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ARCHIVES OF SURGERY

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ORIENTATION TO THE MECHANISMS OF CLINICAL SHOCK

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To the uninitiated the literature on shock is confusing and difficult to understand. As used in the clinical literature of the last thirty years, the term shock has described a clinical picture characterized either by a sharp fall in arterial pressure or by the peripheral signs and symptoms of a decrease in cardiac output. When a physician said that a patient was in shock he was describing the general appearance of the patient. The term had no specific physiologic connotation. It did not indicate why the circulation had failed; it simply implied that it had failed.

From time to time various authors, including ourselves,[1] have attempted to restrict the use of the term shock to the circulatory insufficiency produced by a failure of venous return to the heart. Further work in the clinic has convinced us that a physician many times cannot determine at once the physiologic basis of the circulatory failure. He desires to describe in a word a clinical picture dominated by the peripheral signs and symptoms of circulatory insufficiency, without committing himself to the cause of the circulatory failure. By common use the word shock has become entrenched in this sense, and it does not seem wise or possible to attempt to change its meaning.

On theoretic grounds it is clear that the clinical picture called shock can be produced by failure of one of several portions of the circulation; first, by inability of the heart to pump the normal amount of blood because of weakness of the heart itself; second, by inability of the heart to fill properly because of pericardial tamponade; third, by blocking of the main arterial paths, as in massive pulmonary embolus; fourth by inability of the heart to pump an adequate amount of blood, not because of weakness of the heart but because the venous inflow to the heart has failed; fifth, by generalized failure of cellular metabolism; sixth, by loss of normal vasoconstrictor tone.

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1. Stead, E. A., Jr., and Ebert, R. V.: Shock Syndrome Produced by Failure of the Heart, Arch. Int. Med. **69**:369-383 (March) 1942.

SHOCK PRODUCED BY FAILURE OF THE HEART

An example of shock due to failure of the heart to pump blood is seen in a patient with a rapid heart rate resulting from paroxysmal auricular tachycardia, ventricular tachycardia or auricular flutter. Such a patient may demonstrate all of the classic signs and symptoms of shock. Indeed, when the patient is first seen it may not be at once apparent that poor cardiac action is the basis for the circulatory failure. The heart is not functioning efficiently as a pump because the diastole is too short to allow adequate filling of the heart. The clinician says that the patient is in shock because of the appareance of the patient; the physiologist says that the patient has circulatory insufficiency because of inadequate cardiac output. Slowing of the abnormal cardiac rate improves the patient and cures the shock.

Patients with recent massive myocardial infarctions involving the left ventricle may present the classic manifestations of shock.[1] Some authors have proposed other terms, such as "cardiac collapse,"[2] for this condition, while others use the simple descriptive term shock. The venous return to the heart is normal, but the heart is weakened so that it cannot maintain a normal output of blood. Increasing the venous pressure by transfusions or decreasing it by venesection has little effect on the patient's condition, because the primary disorder is in the heart itself.[1]

In the terminal stages of cardiac failure, no matter what its cause, one may see evidences of

2. Harrison, T. R.: Failure of the Circulation, ed. 2, Baltimore, Williams & Wilkins Company, 1939.

shock superimposed on the manifestations of congestive heart failure. Here, just as in myocardial infarction, the heart itself is at fault, and the symptoms result from diminished cardiac output in the same fashion. A less common type of circulatory disturbance is that seen as the result of certain poisonings, such as acute phosphorus poisoning, in which there appears to be a severe degree of myocardial damage as a result of the direct action of the chemical.[3]

SHOCK CAUSED BY PERICARDIAL TAMPONADE

Acute pericardial tamponade resulting from a stab wound of the heart or from a rapidly forming pericardial effusion causes the typical picture of shock. Pallor, sweating, nausea and restlessness with a low arterial pressure, weak or absent radial pulse and cold extremities present a striking picture of acute circulatory failure. On close observation the venous pressure is found to be increased, but because the neck veins are not dilated, as is frequently the case in congestive failure, the elevated venous pressure may be overlooked. Circulatory impairment occurs because the elevated intrapericardial pressure prevents adequate venous return to the heart. In other words, shock occurs because of blocked inflow to the heart. If either the tamponade is reduced or the venous pressure is elevated, the circulation improves and the evidences of shock disappear.

SHOCK CAUSED BY MASSIVE PULMONARY EMBOLUS

Shock may be produced by blocking the flow of blood through the major arteries. Such a situation is seen in patients with massive pulmonary emboli. Small pulmonary emboli may also be associated with circulatory failure, but it is likely that the mechanism for this type of shock is more complex.

SHOCK PRODUCED BY LOSS OF BLOOD, PLASMA OR FLUID

The clinical picture of shock develops in patients with massive hemorrhage. That this circulatory failure is the result of a decrease in blood volume can be easily proved. Transfusions of blood or plasma restore the circulation to normal.

Hemorrhage may be of many types. It may be external, or it may be internal into body cavities or into tissues. It may be selective. When the capillaries are injured but are not completely broken asunder, as in chemical peritonitis following a ruptured ulcer, in burns or in certain types of crushing injuries, plasma may leak through the injured vessels although the capillary walls still hold the red cells within the vascular bed. This type of selective hemorrhage (loss of plasma) can result in a small blood volume and circulatory failure. That the circulatory failure is produced by the small blood volume is demonstrated again by the immediate response to plasma or whole blood.

In continued vomiting, severe diarrhea or Addison's disease, sufficient electrolytes and water may be lost from the body to produce circulatory failure on the basis of a small blood volume. Administration of isotonic solution of sodium chloride will increase the blood volume and improve the circulation.

Various authors have attempted to distinguish between the mechanism of circulatory failure caused by external hemorrhage and that present in other forms of shock.[4] This distinction seems unwarranted to physicians actually caring for patients. The similar response to an increase in the blood volume of a patient with simple hemorrhage and of a patient with more selective loss of fluid from the blood stream, such as occurs in dehydration or loss of plasma, convinces them that both types of circulatory failure result from a small blood volume. It is true, of course, that the blood tends to be diluted after a hemorrhage and concentrated after a burn, but these differences are the result of the type of fluid lost from the blood stream and are not indicative of a fundamental difference in the mechanism of circulatory failure.

SHOCK PRODUCED BY FAILURE OF CELLULAR METABOLISM

Patients with acute infectious diseases frequently present the clinical picture of shock before they die. Because the usual picture of congestive failure is absent and because the circulation does not improve with administration of digitalis, it is frequently stated that these patients have peripheral circulatory failure or shock and that the circulation has failed because of an inadequate venous return to the heart. Observations were made on a group of patients with the clinical picture of shock produced by acute infections.[5] By staying constantly with all patients admitted to the hospital with an overwhelming infection we obtained data before and during the period of circulatory failure. When the course was unfavorable, the circulation failed,

3. Warren, J. V., and Stead, E. A., Jr.: Unpublished observations.

4. Wiggers, C. J.: The Present Status of the Shock Problem, Physiol. Rev. **22**:74-123 (Jan.) 1942. Blalock, A.: Principles of Surgical Care, Shock and Other Problems, St. Louis, C. V. Mosby Company, 1940.

5. Ebert, R. V., and Stead, E. A., Jr.: Circulatory Failure in Acute Infections, J. Clin. Investigation **20**: 671-679 (Nov.) 1941.

the patient became cold and pale and the pulse pressure narrowed. At this time the physician in charge usually made the diagnosis of peripheral circulatory failure or shock. Studies of the blood of such patients showed that the plasma volume was normal and that there was no evidence of hemoconcentration. The vasomotor centers were functioning normally, as evidenced by the fact that blocking the nerves to a cold extremity caused the extremity to become warmer. These studies eliminated decrease in blood volume or failure of the vasomotor centers as the cause of the circulatory failure. The possibility still existed that the shock might be caused by an inadequate venous return because of pooling of blood in dilated splanchnic veins. If the pooling of blood in dilated veins and a decrease in effective venous pressure in the right atrium were responsible for the circulatory failure, raising the venous pressure would improve the circulation. The venous pressure was therefore recorded by inserting a needle in the external jugular or the femoral vein. Plasma and blood were then given rapidly until the veins of the body were engorged and until the venous pressure was elevated. The circulation did not improve; this demonstrated that the circulatory failure was not caused by an inadequate venous return. The data suggested that the heart was at least in part at fault and that the circulation could not be restored to normal by raising the venous pressure. Other studies showed that none of the circulatory system was functioning normally. The infection had produced metabolic disturbances in cells throughout the body, and the cells were slowly dying. The circulatory failure was secondary to a general failure in metabolism. Treatment with transfusions and digitalis was useless. If the infection could be controlled, the circulation improved. If it could not be, the patient died.

This same picture of shock is not infrequently seen in the medical wards in patients with advanced hepatic destruction due to cirrhosis or metastases, in patients dying with prolonged congestive failure and in patients dying from uremia or malignant hypertension. It is observed in the surgical wards as a manifestation of the circulatory failure which occurs some days after a severe burn or postoperatively in patients who acquire an infection. Unless the underlying metabolic defect can be corrected the patient dies. Treatment directed toward increasing the filling pressure of the heart is without avail.

As pointed out previously, any marked decrease in blood volume, be it from loss of plasma because of local damage to capillaries, from burns, peritonitis or trauma, from loss of blood by hemorrhage or from loss of fluid by dehydration, will cause circulatory failure. This circulatory failure occurs in the presence of a heart which is capable of functioning normally. If the inadequate circulation persists for a sufficient length of time, the circulatory insufficiency is no longer readily reversed by transfusions, and in time the condition becomes completely irreversible.

This condition of irreversible shock has puzzled clinicians and physiologists alike. For a time it was believed that the capillaries throughout the body became more permeable because of the circulatory insufficiency and that the shock became irreversible because any fluid placed in the vascular bed immediately leaked out. This thesis seemed plausible because, with the knowledge that any injury to the capillaries by trauma, burns or chemicals would cause the capillaries in the injured part to become abnormally permeable to protein, it seemed logical that generalized circulatory failure might injure all of the capillaries throughout the body and cause the entire capillary bed, even at a distance from the injury, to leak protein freely. This view was supported by the observation that complete ischemia in a part did cause local damage to and increased permeability of capillaries.

Studies on patients with circulatory failure from trauma, burns and infection have shown that the capillaries distant to the point of injury do not become abnormally permeable to protein because of prolonged circulatory failure.[6] Only the capillaries at the site of injury leak protein freely. The cells of the blood vessels seem to be tougher than the cells in certain other organs, particularly the brain. In generalized circulatory failure, the central nervous system becomes depressed and the respirations stop before the capillaries throughout the body are injured sufficiently to leak protein. Similar observations have been made on the effects of lack of oxygen on the permeability of capillaries. If the capillaries of a part are completely deprived of oxygen, damage to them results and the capillaries in the anoxic part leak protein freely. If an unanesthetized patient is studied, it is found that progressive oxygen unsaturation of the arterial blood causes serious derangement in cerebral function before there is a detectable alteration in the permeability of the capillaries throughout the body.

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6. Stead, E. A., Jr., and Warren, J. V.: The Protein Content of the Extracellular Fluid in Normal Subjects After Venous Congestion and in Patients with Cardiac Failure, Anoxemia and Fever, J. Clin. Investigation **23**:283-287 (March) 1944. Fine, J., and Seligman, A. M.: Traumatic Shock: VII. A Study of the Problem of the "Lost Plasma" in Hemorrhagic, Tourniquet, and Burn Shock by the Use of Radioactive Iodo-Plasma Protein, ibid. **23**:720-730 (Sept.) 1944.

What, then, is the cause of irreversible shock? It appears to be caused by irreversible changes in the metabolism of cells throughout the body because of prolonged circulatory insufficiency. When the circulation is inadequate, none of the cells of the body functions normally. In time these metabolic disturbances become irreversible and the cells begin to die. At this time increasing the venous return to the heart and elevating the venous pressure do not restore the cardiac output to normal. Thus the cells of the heart are also affected, and this in part accounts for the circulatory failure. The situation is similar to circulatory failure caused by infection. In so-called irreversible shock, the cells of the body die because of abnormalities in metabolism produced by prolonged circulatory failure. In uncontrolled infections the cells die because the growth of bacteria has interfered with the enzyme systems of the cells. In neither condition will transfusions restore the circulation to normal.

The relationship between shock which responds to therapy and irreversible shock may be illustrated by a description of the clinical course of a patient with a perforated peptic ulcer.

The patient entered the hospital in shock twelve hours after the perforation. He was pale, sweating and mentally confused and had a low arterial pressure with a narrow pulse pressure. Examination of the blood showed severe hemoconcentration and striking decrease in the plasma volume and the quantity of circulating plasma protein. The circulation failed because the blood volume had decreased to so great an extent that the venous return to the heart was inadequate. The heart was capable of pumping blood, but it was not receiving the blood to pump. This was proved by giving a large infusion of plasma. As the plasma volume rose, the venous return to the heart increased and the circulation rapidly returned to normal. The patient was dramatically improved. The cause of the hemoconcentration and the decrease in the quantity of plasma in the blood stream was not difficult to find. The abdomen contained several liters of fluid which had a protein concentration of about 4 Gm. per hundred cubic centimeters. The chemical irritation caused by the leakage of gastric juice over the peritoneal cavity had altered the permeability of the capillaries, and plasma had leaked from the blood stream into the peritoneal cavity.

The patient was taken to the operating room, and the perforation in the gastrointestinal tract was closed. The condition of the patient remained good for twenty-four hours, but after this time evidence of generalized peritonitis was present and the course from then on was progressively downward. Transfusions of plasma were continued, but the circulation again failed. The patient was once more pale and cold, with a weak, thready pulse. At this time there was no hemoconcentration and the plasma volume was normal. Further transfusions were without value because the circulatory failure was now caused not by a decrease in blood volume but by alterations in cellular metabolism produced by the infection.

SHOCK PRODUCED BY CHANGES IN TONE OF THE SMALL BLOOD VESSELS

Acute circulatory collapse of reflex origin (primary shock or common faint), with or without loss of consciousness, produces the clinical picture of shock. If the circulatory collapse is of short duration and the sweating not excessive, the extremities remain warm. If it is more prolonged, the extremities may become as cold as in any other form of failure of the circulation. When the patient is first seen it may be impossible to decide whether this is a benign state or whether the patient is in a critical condition from loss of blood, pericardial tamponade or acute heart failure.

Recently observations have been made on the state of the circulation during the acute circulatory collapse occurring in blood donors.[7] In spite of the striking pallor and the low arterial pressure, the cardiac output is not decreased. The pressure in the right atrium is not lowered. The circulatory failure is caused by a sharp fall in peripheral resistance, presumably by arteriolar dilatation. It appears as if sensory stimuli from any efferent nerve or from the emotional control of thought may cause a sudden reflex arteriolar dilatation, which results in a sharp fall in the arterial pressure. If the donor is upright, loss of consciousness will occur if the low arterial pressure is inadequate to maintain the cerebral blood flow against the force of gravity. This type of collapse is benign with the person in the recumbent position, because the over-all blood flow in the tissues is not reduced.

The factors responsible for the circulatory failure which can be produced by motionless standing in normal subjects after the ingestion of sodium nitrite [8] and in patients with acute infections and fatigue have never been completely determined. How much of the circulatory failure is caused by venous pooling in veins the tone of which has been decreased by disease or by drugs and how much is the result of arteriolar vasodilatation secondary to reflex stimuli induced by the upright position have never been

7. Barcroft, H.; Edholm, O. G.; McMichael, J., and Sharpey-Schafer, E. P.: Posthaemorrhagic Fainting: Study by Cardiac Output and Forearm Flow, Lancet **1**:489-491 (April 15) 1944. Warren, J. V.; Brannon, E. S.; Stead, E. A., Jr., and Merrill, A. J.: The Effect of Venesection and Pooling of Blood in the Extremities on the Atrial Pressure and Cardiac Output in Normal Subjects with Observations on Acute Circulatory Collapse in Three Instances, J. Clin. Investigation, to be published.

8. Weiss, S.; Wilkins, R. W., and Haynes, F. W.: The Nature of the Circulatory Collapse Induced by Sodium Nitrite, J. Clin. Investigation **16**:73-84 (Jan.) 1937.

demonstrated. It is possible that both mechanisms are important.

A pronounced decrease in arterial pressure without other evidences of circulatory insufficiency is seen after acute bouts of fever produced by malaria or intravenous injection of typhoid vaccine.[9] Occasionally this occurs in other diseases, such as pneumonia. It would appear that the infection causes a loss of arteriolar tone and a lowering of arterial pressure. Quantitative studies on this condition are needed before definite conclusions can be drawn.

Anaphylactic shock causes a distinct fall in arterial pressure and the clinical picture of shock. It is not clear to what degree generalized interference with cellular metabolism or hemoconcentration due to damage to capillaries produces circulatory failure.

GENERAL COMMENT

For the sake of clarity of presentation, the various mechanisms which produce the clinical picture of shock have been described separately. In any given patient several of these disturbances may be present at the same time. Infcetion and a small blood volume frequently occur together. Patients who have lost blood from hemorrhage are prone to have reflex circulatory collapse.

9. Chasis, H.; Goldring, W., and Smith, H. W.: Reduction of Blood Pressure Associated with the Pyrogenic Reaction in Hypertensive Subjects, J. Clin. Investigation **21**:369-376 (July) 1942.

SUMMARY AND CONCLUSIONS

Much of the literature on shock will become clearer if it is remembered that as used by the clinician the term shock has no physiologic connotations. It simply describes a clinical picture dominated by the peripheral symptoms and signs of circulatory failure, which may be produced by weakness of the heart itself, inability of the heart to fill because of pericardial tamponade, blockage of the great arterial pathways, diminished inflow due to insufficient blood volume, generalized failure in cellular metabolism or loss of normal vascoconstrictor tone.

Generalize failure in cellular metabolism is a frequent cause of the shock syndrome. Prolonged circulatory failure from hemorrhage, loss of plasma or dehydration can so damage the metabolic systems of the cells that recovery is not possible, even though the circulation is temporarily restored. This condition is described in the literature as irreversible shock. The products of bacterial growth may likewise cause either reversible or irreversible cellular damage and produce the clinical picture of shock. Circulatory failure secondary to a generalized disturbance in cellular metabolism also occurs in patients with severe burns after the first few days, in patients with severe hepatic damage and in patients with renal failure or prolonged congestive heart failure.

ARTERIOVENOUS FISTULA BETWEEN THE RIGHT COMMON ILIAC ARTERY AND THE INFERIOR VENA CAVA

REPORT OF A CASE OF ITS OCCURRENCE FOLLOWING AN OPERATION FOR A RUPTURED INTERVERTEBRAL DISK WITH CURE BY OPERATION

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Numerous cases of traumatic arteriovenous fistula in which cure was obtained by surgical measures have been recorded in the literature. The abnormal physiologic effects produced by this condition have been thoroughly studied and reported by Reid,[1] Holman,[2] Makins [3] and Matas,[4] to whose writings the reader may refer. Large fistulas involving the major arteries and veins when allowed to persist result in gradual cardiac hypertrophy, dilatation and finally failure, and if they are not corrected death results. The first symptom that may develop is gradually increasing dyspnea on exertion. This is a warning of impending cardiac decompensation that should not be ignored.

The diagnosis of an acquired arteriovenous fistula is not difficult in the majority of cases. In an extremity a pulsating expansile mass is found in the region of the fistula. The limb frequently enlarges and on its surface many large engorged pulsating veins are seen. A continuous bruit and thrill with systolic accentuation over the pulsating mass are pathognomonic of an arteriovenous fistula. An immediate drop in the pulse rate following occlusion of the fistula by direct pressure over it (Branham's bradycardiac reaction) is characteristic of the condition. This is a useful test to differentiate a fistula from a true aneurysm.

The purpose of this paper is to present a case of arteriovenous fistula between the right common iliac artery and the inferior vena cava following an operation for a ruptured intervertebral disk. Injury to the blood vessels was not recognized at the time of the operation on the disk, and the diagnosis of the fistula was not made until eight months later, when the patient complained of increasing dyspnea on exertion.

REPORT OF A CASE

C. J. G., a draftsman, was admitted to the Massachusetts General Hospital, Baker Memorial, on April 30, 1943, complaining of shortness of breath on exertion.

Present Illness.—On Sept. 23, 1942 he had a ruptured intervertebral disk removed and a spinal fusion done at another hospital for pain in the back and legs. Since that operation he had not been completely well, although his pain was relieved. In January 1943 he returned to work. He noticed slight edema of the ankles in the evening, which disappeared by morning. He felt fairly well until February, when he first noticed fatigue during the day's work. In March he noted moderate dyspnea on walking fast or climbing stairs, which before did not bother him. He saw three physicians, all of whom diagnosed his condition as some type of cardiac disease. On March 15 he had several severe nosebleeds.

Past History.—His past history was essentially noncontributory; there was no history of rheumatic fever, chorea or tonsillitis. He had had no serious illnesses except severe pain in the back of five years' duration, for which he had an intervertebral disk removed and a spinal fusion done.

Physical Examination.—Examination showed a well developed and nourished, alert, cooperative patient. Neck: The veins of his neck were distended and exhibited deep pulsations. Lungs: The breath sounds were normal, with no rales. Heart: The heart was enlarged to the left; the left border of dulness at the apex was 11 cm. from the midline in the fifth interspace. The apex impulse was forceful and 3 cm. beyond the midclavicular line. The heart sounds were of good quality with a systolic murmur and a precordial protodiastolic gallop rhythm. The pulmonic second sound was greatly accentuated. A diastolic murmur was heard. The pulse rate was 100 and Corrigan in type. The blood pressure was 140 systolic and 40 diastolic. Prior to the operation on the disk his blood pressure was 120 systolic and 80 diastolic, and at the termination of the operation it was 85 systolic and 75 diastolic. Abdomen: Abdominal examination gave negative results except for a continuous thrill with systolic accentuation felt in the right femoral region and in the lower portion of the abdomen below the umbilicus. Auscultation revealed a loud continuous bruit with systolic accentuation, which was audible over the entire abdomen and over the course of the vessels of the right lower extremity, but not of the

From the Departments of Surgery and Medicine, Massachusetts General Hospital.

1. Reid, M. R., and McGuire, J.: Arteriovenous Aneurysms, Ann. Surg. **108**:643, 1938.

2. Holman, E.: Arteriovenous Aneurysm, New York, The Macmillan Company, 1937.

3. Makins, G. H.: Gun Shot Injuries to the Blood Vessels, New York, William Wood & Company, 1919.

4. Matas, R.: Some Experiences and Observations in the Treatment of Arteriovenous Aneurysms by the Intrasaccular Method of Suture (Endo-Aneurismorrhaphy) with Special Reference to the Transvenous Route, Ann. Surg. **71**:403, 1920.

left. The same bruit was heard over the lumbar and the lower thoracic portion of the spine. It was loudest over the lower lumbar region. Extremities: There were normal pulsations in all the peripheral arteries, including the dorsalis pedis and the posterior tibial arteries of both feet. The pulsations in the right leg were diminished as compared with those in the left.

Laboratory Studies.—The red blood cell count was 4,330,000, with a hemoglobin content of 12 Gm. per hundred cubic centimeters. The white cell count was 7,600. A smear showed 70 per cent polymorphonuclear cells, 24 per cent small lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. The platelets were normal, and the red blood cells showed achromia with some variation in size and shape. The blood nonprotein nitrogen content was 38 mg. per hundred cubic centimeters. A Hinton test on the blood gave a negative reaction. The vital capacity was 2.9 liters, or 68 per cent of normal. Examination of the urine showed a specific gravity of 1.028, a moderate trace of albumin and no sugar or diacetic acid. The sediment showed occasional casts, 2 red blood cells and 4 white blood cells per high power field. An electrocardiogram showed normal rhythm, with a rate of 100, a PR interval of 0.2 second, upright T waves and a slight deviation of the axis to the left. It was considered within normal limits except for the slightly prolonged PR interval.

Roentgenographic Examination.—Examination of the chest by Dr. Laurence L. Robbins showed a prominence of vascular shadows, particularly in the hilar region. The pulmonary fields were otherwise clear. The heart showed generalized enlargement, which was more marked in the region of the left ventricle. The measurements were 16.6 by 30.0 cm. The left auricle was not dilated. The pulsations of the heart, observed fluoroscopically, were not of the Corrigan type, but there was a wavelike character to the pulsations of both the aorta and the heart, which was similar to that of the venous pulsations in the engorged veins. There was definite evidence of pulsations in the liver. Examination of the lumbar portion of the spine showed no evidence of erosion. The spinous processes of the fourth and fifth lumbar vertebrae were partially resected, and there was narrowing of the fourth lumbar disk space.

Diagnosis.—A diagnosis of traumatic arteriovenous fistula between the right common iliac artery and the inferior vena cava was made.

Course.—The patient was digitalized.

First Operation.—On May 8, 1943, with the patient under ether anesthesia administered by the endotracheal route, through a right flank incision the first, second, third and possibly fourth lumbar ganglions were removed. There was a great deal of thickening and fibrosis, so that isolation of the ganglions was a little more difficult than usual. The vena cava was visualized, and it also seemed considerably thickened and surrounded with some scar tissue. A continuous thrill was palpable in it. There was no excessive bleeding or large venous vessels other than normal in this location. The wound was closed in layers. Cotton ligatures and sutures were used throughout.

The patient made a good postoperative recovery. The right foot and leg were dry and warm throughout, as compared with the left leg and foot, which were cool and moist. On May 18 a Miller-Abbott tube was passed and advanced into the small intestines to deflate them.

Second Operation.—On May 19, 1943, with the patient under ether anesthesia administered by the endotracheal route, the abdomen was opened through a right paramedian incision. The abdominal contents were normal except for pulsations in the liver. The bifurcation of the aorta and that of the vena cava were exposed by opening the posterior portion of the peritoneum over them. A pronounced continuous thrill with systolic accentuation was palpable over both these vessels and extending down through the right iliac vessels. It could be obliterated by finger point compression over the proximal end of the right common iliac artery. The fistula lay opposite the intervertebral space between the bodies of the fourth and fifth lumbar vertebrae. The aorta was first dissected free. It was surrounded with considerable scar tissue. A tourniquet clamp was placed around it. The left and the right common iliac artery were isolated and similar clamps placed around them. It was then possible to place another tourniquet clamp around the right common iliac artery just proximal to the fistula (fig. 1). Next an attempt was made to dissect free the right common iliac vein, which was enormously dilated, but because of scar tissue dissection was difficult, and a hole was torn in the vein. There was considerable loss of blood at the time, but by occluding the aortic tourniquet and the distal one around the right common iliac artery the bleeding was readily controlled with a little pressure. An attempt was then made to free the left common iliac vein, but this was impossible also, because it was so adherent to the scar tissue. Finally it was decided that therapeutic venous occlusion could be obtained by interrupting the right external iliac vein. It was ligated in continuity just distal to its junction with the hypogastric vein. The right common iliac artery was doubly ligated distal to the bifurcation of the aorta

Fig. 1.—A retouched photograph showing the transperitoneal exposure of the bifurcation of the aorta and of the inferior vena cava. The site of the arteriovenous fistula, between the right common iliac artery and the inferior vena cava, is shown. The numbers 1, 2, 3 and 4 designate the location of the tourniquet clamps and the order in which they were applied. The arterial inflow was controlled first by application of the first tourniquet around the aorta. The arterial inflow from the collateral circulation was controlled next by applying the second and the third clamp, respectively, around the left common iliac artery and the right common iliac artery distal to the fistula. Finally the fourth tourniquet was applied to the right common iliac artery proximal to the fistula, thereby isolating the portion of that artery which contained the fistula. Note the huge size of the inferior vena cava and the right common iliac vein and the so-called venafication [1] of the right common iliac artery.

and proximal to the fistula. It was then divided, and an additional stitch ligature of cotton was placed distal to the silk ligature. The right common iliac artery was similarly treated distal to the fistula. Fortunately, it was possible to do this just proximal to its bifurcation, so that the hypogastric artery was not disturbed. The tear which had been made in the huge right common iliac vein was then closed with a running suture. The portion of the right common iliac artery containing the fistula was left attached to the inferior vena cava (fig. 2). It was felt unnecessary to resect it, since it had no tributaries which might if present have led to a recurrence. A definite arterial pulsation was noted in the distal ligated end of the right common iliac artery, indicating an excellent collateral arterial blood supply. The posterior portion of the peritoneum was closed with a running suture of no. 000 chromic catgut. The abdominal wound was closed in layers without drainage.

The operation required three and one-half hours. During the operation and in the immediate postoperative period he received 1,000 cc. of citrated blood. This was given because his blood pressure fell to 90 systolic and 60 diastolic near the termination of the operation. His pulse dropped from 120 beats per minute to 70 immediately after the proximal and the distal ligation of the right common iliac artery, which eradicated the fistula (fig. 3).

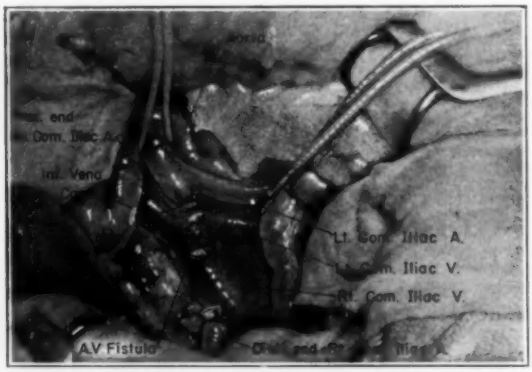

Fig. 2.—A retouched photograph to show the arrangement of the vessels at the completion of the operation. The right common iliac artery was divided and ligated both proximal and distal to the fistula. The portion of the artery containing the fistula was left attached to the inferior vena cava after ligation of both ends. Note the normal size of the ligated distal end of the right common iliac artery, with pulsations, indicating an adequate collateral arterial blood supply. The next step in the operation was closure of the posterior portion of the peritoneum over these vessels.

Postoperative Course.—Heparin was given by the continuous intravenous drip method for forty-eight hours, the clotting time being maintained between twenty and thirty-five minutes. Administration was stopped after that time, because it was obvious that the circulation of his right lower extremity was adequate.

On May 22, the third postoperative day, pulsations were first noted in the right dorsalis pedis and posterior tibial arteries. They were also present in the right femoral and popliteal arteries. The pulse in these vessels was not of the same caliber as that of the pulse in the vessels of the left leg. The blood pressure in the right arm was 148 systolic and 80 diastolic; in the left leg it was 180 systolic and 80 diastolic and in the right leg 110 systolic; no diastolic sound could be heard in the right leg.

On May 25 the patient complained of heaviness in his right thigh, and examination showed tenderness in the right groin extending down Hunter's canal. There was no pain in the calf; the whole leg was a little swollen and bluish. A diagnosis of thrombosis in the iliac and the femoral vein was made, and treatment with dicoumarin (3,3'-methylenebis [4-hydroxycoumarin]) was started. He received one dose of 300 mg. and in two days an additional 100 mg. The prothrombin clotting time remained in the neighborhood of sixty seconds following administration of this drug; hence its use was discontinued. As the prothrombin time was still prolonged on June 1, he was given 3.2 mg. of menadione bisulfite intramuscularly.

On May 27 another roentgenogram of the chest, taken by Dr. Robbins, showed distinct improvement in the appearance of the heart and pulmonary fields. The pulmonary vascular congestion had completely disappeared. The heart was much smaller, with a transverse diameter of 14.6 by 28.3 cm. It was still slightly enlarged, however, the normal size for a patient of his height and weight being 12.5 cm.

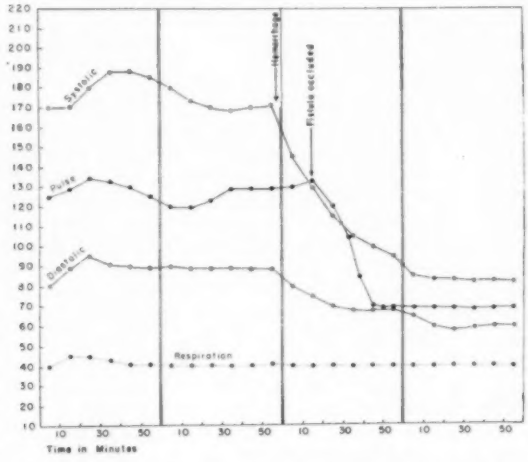

Fig. 3.—A reproduction of the anesthesia chart, showing the pulse and respiratory rates and the blood pressure during the operation. Note the fall in the blood pressure following the hemorrhage which occurred at the time the right common iliac vein was inadvertently torn and also the decided drop in the pulse rate (Branham's bradycardiac reaction) which was observed when the fistula was eradicated.

On June 6 the patient was up, walking and anxious to go home. His general condition seemed good, and the circulation of his leg was adequate; so he was discharged from the hospital on this day.

After the patient's discharge from the Massachusetts General Hospital, Baker Memorial, he began raising foul-smelling sputum and had a low grade fever. On June 16 he was admitted to the New Haven Hospital (New Haven, Conn.), under the care of Dr. Gustaf E. Lindskog. A roentgenogram showed a large encapsulated pyopneumothorax on the left side of the chest between the lower and the middle lobe. It was felt that the origin of the empyema was secondary to a septic pulmonary infarction. The origin of the thrombus, which produced the infarction, was probably at the site of the arteriovenous fistula, where the rent in the right common iliac vein had to be sutured.

Fatal pulmonary embolism probably had been prevented by interruption of the external iliac vein at the time of the operation.

On Aug. 18, 1944 the patient returned for a check-up. He stated that he was feeling well except that he had some cramps in the calf of his right leg at night. He also noticed that if he walked several miles his right leg seemed to tire more easily than his left, but he did not suffer severe intermittent claudication. He stated that he had been inducted into the Army of the United States but had been discharged because he was over 28 years of age and not because of the condition of his right leg. Physical examination at this time showed a normal-sized heart with a blood pressure of 120 systolic and 90 diastolic. Oscillations in his right calf, measured with a Tycos sphygmomanometer, were 1 mm. at 120 mm. of pressure, and in his left calf they were 3 mm. There was no atrophy of the right lower extremity, as measurements of the two legs were the same. There still were palpable pulsations in the right femoral, popliteal, dorsalis pedis and posterior tibial arteries.

Other Studies on the Circulation.—The pressure in the left antecubital vein before operation was 180 mm. of water above the right auricle; after operation it was 150 mm. The circulation time, as determined in the antecubital vein from the arm to the tongue preoperatively with calcium gluconate, was twenty seconds, and with ether from the arm to the lung it was eight seconds; postoperatively with calcium gluconate from the arm to the tongue it was twelve seconds, and with ether from the arm to the lung it was four seconds.

COMMENT

This case demonstrates a number of interesting points, which justifies its publication. It reveals that surgical removal of a ruptured intervertebral disk is not without danger to the great vessels which lie on the anterior surface of the bodies of the lumbar vertebrae, and it demonstrates that the common iliac artery can be interrupted without endangering the viability of the limb. Anatomic study of this region shows that the inferior vena cava is formed by the union of the two common iliac veins to the right of the median plane in front of the body of the fifth lumbar vertebra and behind the right common iliac artery. The latter crosses the distal end of the vena cava opposite the fourth interverterbral disk from right to left, and owing to the greater turgidity of the artery it fixes the vena cava to a certain extent against the vertebral column. As a result of this anatomic arrangement of the right common iliac artery, the inferior vena cava and the fourth intervertebral space, a sharp curet or instrument, such as is used for removal of a ruptured intervertebral disk, may transfix the artery and vein if suddenly forced through the anterior longitudinal vertebral ligament (fig. 4). Although in this patient the surgeon did not recognize that his instrument had injured these vessels, there seems little doubt that the fistula was produced in this manner. According to Mixter,[5] Talmadge[6] and Walker,[7] similar lesions have been produced by other surgeons while they were performing operations for ruptured intervertebral disks.

It appears offhand that such a vascular lesion would result in severe uncontrollable hemorrhage. An analysis of the situation, however, reveals that the blood escaping from the common iliac artery will follow the path of least resistance. Since the venous pressure in the inferior vena cava is approximately zero, escaping arterial blood will naturally flow into the large venous reservoir of the caval system rather than extravasate into the prevertebral spaces against resistance of the tissues. There was undoubtedly some local extravasation, as evidenced by the abnormal fibrous tissue around the great

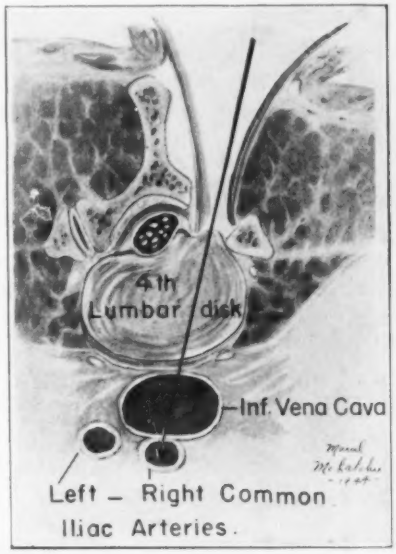

Fig. 4.—A diagrammatic drawing to show a cross section of the anatomic structure at the level of the fourth lumbar disk and the operative exposure to remove the ruptured disk. The arrow demonstrates the mechanism by which the fistula was produced. The curet transfixed the inferior vena cava and pierced the posterior wall of the right common iliac artery.

vessels found at operation, but it could not have been massive in the absence of shock following the operation.

The diagnosis of arteriovenous fistula was made in this case because of the beginning cardiac decompensation, the enlargement of the heart with a characteristic type of pulsation observed on fluoroscopic examination, and the

5. Mixter, W. J.: Personal communication to the authors.

6. Talmadge, S.: Personal communication to the authors.

7. Walker, A. E.: Personal communication to the authors.

continuous thrill with a systolic accentuation, which was heard loudest over the region of the lumbosacral articulation. The site of the fistula was localized preoperatively between the right common iliac artery and the inferior vena cava, because the thrill and the bruit were transmitted through the vessels of the right leg but not the left and the thrill was heard cephalad over the course of the inferior vena cava. Since the right common iliac artery crosses the distal end of the inferior vena cava from the left of the midline to the right side, it seemed most probable that the fistula was between these two vessels. The findings at operation proved this assumption to be correct.

In cases of this type, eradication of the arteriovenous fistula is the most important goal in the operative treatment, since the cardiovascular system will be restored to normal and thereby relieve the heart of the extra burden which it is carrying. Preservation of the circulation in the extremity is of second importance but none the less an objective to be attained. Therefore, the ideal to be achieved by surgical treatment is the accomplishment of both these aims. Eradication of the fistula in this case necessitated interruption of the right common iliac artery, thereby jeopardizing the circulation of the right lower extremity. According to the stastistics of some authorities,[8] the incidence of gangrene or other disturbances may be as high as 50 per cent following sudden ligation of the common iliac artery. Halsted,[9] to the contrary, after a careful analysis of 30 reported cases of ligation of the common iliac artery, concluded that gangrene was likely to occur in about 6 per cent. He made the observation, however, that most of the patients who survived complained of severe cramps in the leg on walking a short distance. Fortunately, our patient's cardiac condition was not critical, so that it was possible first to safeguard the circulation of the leg without endangering seriously his life and later to eradicate the fistula.

The operative treatment was carried out, therefore, in two stages. The first was directed toward increasing the collateral blood supply of the extremity, so that when the common iliac artery was divided at the second stage the arterial circulation would be adequate to prevent ischemia and gangrene. It consisted of a sympathectomy in which the first, second and third lumbar ganglions on the right side were removed. This produced maximum permanent vasodilatation in the right leg from the toes to the groin by abolishing all the vasoconstrictor impulses from the central nervous system to the vascular system of the extremity. The importance of this step cannot be overemphasized. The second stage was carried out ten days after the sympathectomy, because it has been demonstrated by Smithwick[10] that there is a temporary period of vasoconstriction following the initial vasodilatation after ablation of the sympathetic ganglions. The effect is noticeable within forty-eight hours after the sympathectomy, and the maximum permanent vasodilatation is not stabilized for five or six days longer. For this reason it is important to delay elective operations on major arteries until this stabilization after the sympathectomy has occurred.

The collateral circulation was further augmented at the second stage by therapeutic venous occlusion, since there is both experimental[11] and clinical[12] evidence to prove that simultaneous ligation of the concomitant vein, when the major artery to a limb is ligated, will increase the flow of blood to the extremity and reduce the incidence of gangrene. Accordingly, in this case the external iliac vein was isolated and ligated in continuity. When exposed it was found to be of normal size, which indicated that most of the blood escaping through the fistula traveled back through the tremendously enlarged vena cava to the heart. An additional reason for interrupting the external iliac vein was to prevent fatal pulmonary embolism, since trauma to the common iliac vein caused by the operative procedure might result in intravascular thrombosis. With the long venous channel to the thigh interrupted, the chance of a fatal pulmonary embolus was greatly

8. Burns, Shock, Wound Healing and Vascular Injuries, Military Surgical Manuals, National Research Council, Philadelphia, W. B. Saunders Company, 1943, vol. 5.

9. Halsted, W. S.: The Effect of Ligation of the Common Iliac Artery on the Circulation and Function of the Lower Extremity, Bull. Johns Hopkins Hosp. **23**:191, 1912.

10. Smithwick, R. H.: Surgical Intervention on the Sympathetic Nervous System for Peripheral Vascular Disease, Arch. Surg. **40**:286 (Feb.) 1940.

11. Holman, E.: (*a*) Surgery of Large Arteries, Ann. Surg. **85**:173, 1927. Holman, E., and Edwards, M. E.: (*b*) New Principle in Surgery of the Large Vessels, J. A. M. A. **88**:909, (March 19) 1927. Linton, R. R.; Morrison, P. J.; Ulfelder, H., and Libby, A. L.: Therapeutic Venous Occlusion, Am. Heart J. **21**:721, 1941. Pearse, H. E.: A New Explanation of the Improved Results Following Ligation of Both Artery and Vein, Ann. Surg. **86**:850, 1927.

12. Linton, R. R.: Treatment of Acute Arterial Occlusion by Means of Intermittent Venous Occlusion, Arch. Surg. **46**:395 (March) 1943. Pemberton, J. D., and McCaughan, J. M.: Traumatic Lesions of Arteries: Indications for the Therapeutic Ligation of Veins, Ann. Surg. **96**:1103, 1932. Makins.[8]

reduced. It is felt that the patient's life was probably saved by this step, since a minor pulmonary infarction did develop following the operation.

The second stage was the operation to eradicate the arteriovenous fistula. According to the literature,[13] the method of choice is excision of the fistula and the vessels involved after ligation and division of the artery and vein proximal and distal to it. It was impossible to carry out this procedure in this case, because the tremendous enlargement of the inferior vena cava and the right common iliac vein made it impossible to free either for the purpose of ligation. In addition, it was considered unnecessary because of the type of operation that was performed and also since the preliminary sympathectomy of the lumbar ganglions had been carried out to safeguard the circulation of the extremity.

Direct adequate exposure in the surgical treatment of large blood vessels is the sine qua non of success. For this reason a transperitoneal approach was utilized. The abdomen was opened through a right paramedian incision. The intestines had been deflated by a Miller-Abbott tube, so that they were readily displaced upward to expose the region of the bifurcation of the aorta and of the inferior vena cava. The fistula was localized by digital pressure over the right common iliac artery. The opening could be palpated readily through the anterior wall of the artery and occluded by pressure with the tip of the index finger. The posterior portion of the peritoneum was incised to expose the lower end of the aorta, the entire length of the right common iliac artery and the proximal end of the left common iliac artery. The right ureter was displaced lateralward. Before an attempt to dissect out the vessels at the site of the fistula was made, control of the arterial inflow both proximal and distal to it was obtained. First, a tourniquet clamp (fig. 1) was applied to the aorta just proximal to its bifurcation. Then similar clamps were placed on the proximal end of the left common iliac artery and on the right common iliac artery distal to the fistula to prevent reflux of blood from the collateral circulation. By closing all three clamps it was then possible to shut off completely the arterial blood flow through the fistula.

Dissection of the right common iliac artery was therefore possible with relative safety and peace of mind, despite an unusual amount of scar tissue about the great vessels in this region. Exploration of the proximal end of the right common iliac artery revealed that the fistulous opening lay about 1.5 cm. from the aortic bifurcation. It was possible to separate this portion of the common iliac artery from the underlying inferior vena cava, so that a fourth tourniquet clamp could be applied at this point; thus the portion of the right common iliac artery containing the fistula was isolated between two clamps.

The fistula was eradicated from the circulation by ligation and division of the right common iliac artery proximal and distal to it. The isolated portion of the right common iliac artery, which contained the fistula, was about 2 cm. in length. It was left in situ attached to the inferior vena cava, resection of it being unnecessary because there were no collateral branches entering it, which if present might cause a recurrence (fig. 2).

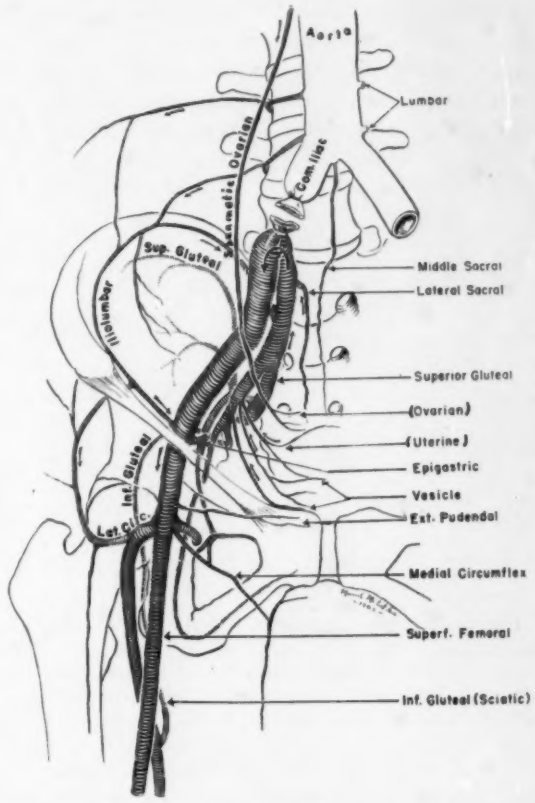

Fig. 5.—A diagrammatic drawing to show the sources of the collateral arterial blood supply to the lower extremity following interruption of the common iliac artery. These consisted of two groups of arteries: (1) the hypogastric artery and its tributaries of the ipsilateral and the contralateral side of the body, namely, the iliolumbar, lateral sacral, superior and inferior gluteal, internal pudendal and superior and inferior vesicle arteries and (2) the inferior epigastric, superficial epigastric, deep circumflex iliac and superficial circumflex iliac arteries.

13. Elkin, D. C.: Vascular Injuries of Warfare, Ann. Surg. **120**:284, 1944. Holman.[2] Makins.[3] Reid and McGuire.[1]

Preservation of the collateral circulation after division of a major artery to an extremity is of vital importance in the prevention of gangrene. Since there are no tributaries of any significance arising from the right common iliac artery between its origin and termination, interruption of it will not interfere with the collateral circulation to the lower extremity providing its bifurcation into the external iliac and the hypogastric artery is preserved. In this case extreme care was taken not to damage this major bifurcation, since preservation of it permits arterial blood, which enters the hypogastric artery through its numerous tributaries by anastomoses from the same and the contralateral side of the body, to pass directly into the external iliac artery and then peripherally through the main arterial system of the extremity. If both the external iliac

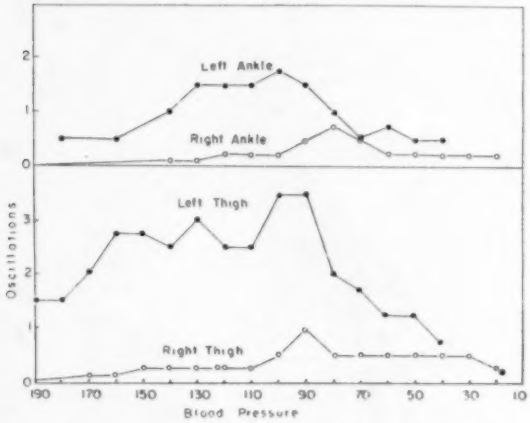

Fig. 6.—Graphs to show the oscillometric readings on the patient's legs two weeks after eradication of the fistula, which confirm the clinical observation that pulsations were detectable in the right posterior tibial and the dorsalis pedis arteries. The oscillations in the right leg were of much less caliber than those in the left, with its normal arterial system, but the fact that they were present and measurable, even with the main artery to the extremity interrupted, should not be overlooked.

and the hypogastric artery are interrupted reflux of arterial blood from the latter, which is the major portion of the collateral arterial supply, is prevented. This predicates a reversal of the flow of blood through the hypogastric artery. An analysis of the hemodynamics under these conditions supports this theory. After ligation of the common iliac artery the arterial blood pressure falls considerably distal to the point of interruption. Owing to the lowered pressure, blood enters the arterial tree through any and all channels connected with it, in which the pressure is at a higher level. Examination of the anatomic structure of these collateral channels (fig. 5) reveals that the main arteries through which blood can enter may be divided into two groups: (1) the hypogastric artery and its tributaries and (2) the tributaries of the external iliac artery, namely, the inferior epigastric, superficial epigastric, deep circumflex iliac and superficial circumflex iliac arteries. The tributaries of the hypogastric artery, which contribute to the collateral blood supply, are the iliolumbar, lateral sacral, superior and inferior gluteal, internal pudendal and superior and inferior vesicle arteries. Blood will enter these not only through anastomoses on the same side of the trunk but through anastomoses with the arteries on the opposite side of the body.

Fig. 7.—A photograph showing the patient's legs two weeks after interruption of the right common iliac artery. The right leg appears normal except for slight muscular atrophy. The bandage covers the scar of the abdominal incision, made to expose the great vessels and the fistula.

Since interruption of the major artery to an extremity causes a pronounced fall in the arterial blood pressure and a decrease in the rate of the flow of blood distal to the point of ligation, spontaneous thrombosis is likely to occur. For this reason, in order to safeguard the collateral circulation of the extremity, heparin was administered intravenously for forty-eight hours following the second stage of the operation. Ad-

ministration was stopped at the end of this time, after it was ascertained that the arterial circulation to the foot was adequate. The coagulation time of the blood was maintained approximately at thirty minutes.

Palpable pulsations were observed in the right dorsalis pedis and the posterior tibial artery for the first time four days following eradication of the fistula. This in itself indicated the adequacy of the collateral circulation. This observation was confirmed by the oscillometer (fig. 6). The presence of pulsations in these peripheral arteries, despite interruption of the main arterial supply to the extremity, is best explained by the fact that arterial blood was entering the main arterial system of the extremity through all arterial tributaries distal to the point of ligation. The total amount of arterial blood thus entering the external iliac and the femoral artery was sufficient in volume to produce pulsations distal to the point of arterial interruption.

The ability of our patient to walk several miles without intermittent claudication fifteen months after interruption of the common iliac artery is additional evidence of the adequacy of the collateral arterial circulation. Halsted,[9] in an analysis of the cases which he studied, noted that in several of them, including 1 of his, the patients were incapacitated because of cramp-like pain in the limb on walking short distances, which he attributed to ischemia. The adequacy of the circulation in the limb in the case reported here was in part due to ablation of the first, second and third lumbar ganglions, which abolished vasoconstrictor impulses and maintained a constant state of maximum vasodilatation.

CONCLUSIONS

Injury to the inferior vena cava and the right common iliac artery may occur during the radical removal of a ruptured intervertebral disk between the fourth and fifth lumbar vertebrae. An arteriovenous fistula between these two vessels may be produced by an instrument which is forced through the anterior longitudinal ligament, transfixing the inferior vena cava and the posterior wall of the right common iliac artery. Serious hemorrhage at the time of the accident may not occur, so that the arteriovenous communication may exist for some time before it is recognized. The first symptoms of its presence may be those of cardiac decompensation.

Ligation and division of the common iliac artery proximal and distal to the fistula were sufficient to cure the condition and reestablish the cardiovascular system to normalcy.

Interruption of the common iliac artery is apparently compatible with adequate circulation and practically normal function of the lower extremity if a preliminary sympathectomy, in which the first, second and third lumbar ganglions are removed, has been carried out.

Therapeutic venous occlusion by simultaneous interruption of the external iliac vein was probably an added factor in establishing the collateral circulation immediately after interruption of the common iliac artery.

TRAUMATIC HEMOTHORAX

DECORTICATION IN THE TREATMENT OF THE CHRONIC UNINFECTED TYPE

MAJOR FRANK P. COLEMAN

MEDICAL CORPS, ARMY OF THE UNITED STATES

The respiratory disability associated with the later stages of wounds of the thorax incurred during war is a real problem. Infection is primarily responsible for the disability in the majority of cases; however, organization of blood within the pleural cavity unattended by sepsis is not uncommon and often leads to an even greater degree of respiratory invalidism. Favorable experiences in the surgical management of the latter condition by decortication of the lung has prompted this communication.

The trend of treatment of acute traumatic hemothorax in this war has been conservative.[1] In the forward zones of combat modern methods of preventing and relieving shock are efficiently executed, thus saving many lives. Respiratory distress is readily recognized and relieved by aspiration of blood without replacement with air. In the forward higher echelons the pleural cavity is emptied of the bloody effusion as soon as possible by repeated aspiration without replacement with air.[2] There is some evidence to support the thesis that the sooner the blood is removed from the pleural cavity the less is the chance of septic complications.[3] On the other hand, the sequence of events precipitated by the presence of blood within the pleural cavity does not warrant the conclusion that early aspiration will prevent the deposition of fibrin. It is the organization of deposits of fibrin which leads to the later varying degrees of respiratory disability in an otherwise uncomplicated acute traumatic hemothorax.

MECHANISM OF THE DISABILITY

When blood escapes into the pleural cavity it apparently undergoes early formation of a clot. The views expressed by Elliott[4] offer an explanation for what appears to be the absence of clotting of blood within the pleural cavity. The author stated "that the effused blood very rapidly passes through the clotting process, but that the coagulation is interfered with by the respiratory movements so that the fibrin is to a considerable extent whipped out of the blood." If bleeding into the pleural cavity is slow, the blood is readily deprived of fibrin by the movements of the diaphragm and the heart. The pleura is irritated by the blood, and an effusion is poured out. The blood free of fibrin mixes with the effusion, resulting in a fluid hemothorax, which does not undergo formation of a clot on removal from the pleural cavity. The fibrin is usually deposited in a dependent location. If bleeding into the pleural cavity is rapid, sufficient agitation may not be present to bring about defibrination of the blood, and a solid hemothorax results. Other factors which favor formation of a massive clot within the thorax are extensive destruction of tissue and retention of foreign bodies within the pleural cavity.

The pleura is able to cope with the deposit of fibrin in a small hemothorax. The associated effusion is either aspirated or absorbed. In such cases no functional incapacity results. On the other hand, deposition of fibrin accompanied by a process of organization may be sufficient to lead to the formation of dense pleural adhesions. The mobility of the diaphragm, thoracic wall and lung is restricted. In such cases a routine roentgen film may reveal only slight haziness over the base of the lung; however, the limitation of the motion of the diaphragm is readily obvious during fluoroscopy, and a deposit of fibrin may be identified in the costovertebral sulcus by suitable lateral roentgenograms of the chest. The mechanism of the disability associated with the organization of a large hematoma within the pleural cavity is obvious. The thick wall of the hematoma fixes the pleural surface of the ribs, thereby interfering with the normal widening of the intercostal spaces during inspiration. Organized

1. Kirk, N. T.: Surgical Care of the Wounded in the U. S. Army, Surgery **15**:211 (Feb.) 1944.

2. (*a*) Edwards, A. T.: Traumatic Hemothorax, Lancet **1**:97 (Jan. 23) 1943. (*b*) Linberg, B. E.; Matsyev, I. E., and Acutin, M. N., cited, Traumatic Hemothorax, editorial, ibid. **1**:315 (March 4) 1944. (*c*) Nicholson, W. F., and Scadding, J. G.: Penetrating Wounds of the Chest: A Review of 291 Cases in the Middle East, ibid. **1**:300 (March 4) 1944.

3. Edwards.[2a] Nicholson and Scadding.[2c]

4. Elliott, T. R.: Gunshot Wounds of the Chest, Brit. M. J. **1**:442 (April 12) 1919.

fibrous tissue contracts, drawing the ribs closer together, and the normal longitudinal curves of the ribs are lost. The involved hemothorax becomes flattened and immobile. The diaphragm when involved loses its function entirely. The involved portion of the lung is usually normal, but it cannot perform its function when it is confined in a fibrous encasement.

THE DISABILITY

The temporary disability associated with uncomplicated hemothorax has been attributed to the organization of fibrin within the pleural cavity. Pain and shortness of breath are the primary symptomatic manifestations. I have observed repeatedly persistence of pain in the chest following what appeared to be otherwise successful treatment of acute hemothorax. Dyspnea was not a prominent symptom. Detailed roentgenograms and fluoroscopic examination of the chest as a rule revealed some fixation of the diaphragm and a deposit of fibrin in the costovertebral gutter. Recent reports have revealed that patients with acute uncomplicated hemothorax do not return to military duty for three months and that the majority complain of pain in the chest for an additional three months.[2c] The symptomatic manifestations and the disability associated with obvious chronic organized hemothorax do not require a great deal of comment. Patients with this complication are unfit for military duty. They are chronically ill. A low grade fever is usually present, and even in the absence of infection the temperature may reach a daily level as high as 102 F. There is distinct pallor to the skin, and frequently secondary anemia is present. Dyspnea on exertion and pain in the involved side of the chest are common symptoms. The hemothorax is flattened and immobile. There is compensatory emphysema of the uninvolved lung. The compensatory activity of the contralateral lung exaggerates the deformity produced by the chronic organized hemothorax.

INCIDENCE OF CHRONIC UNINFECTED HEMOTHORAX

It is difficult to come to any conclusion relative to the frequency of formation of a massive blood clot within the pleural cavity. Only sporadic cases appear in the literature. Infected hematomas have been treated as empyema and classified in the literature under septic hemothorax. Meakins and Walker [5] were the first to point out the close connection between the development of deformity of the chest and the time that the pleural cavity was allowed to retain the fluid, irrespective of whether the fluid was sterile or infected. These authors cited 3 cases in which soldiers were given a medical discharge from the army on account of invalidism which was produced by the organization of blood within the pleural cavity. During World War I Elliott [6] reported an incidence of 3 cases of formation of a massive uninfected clot in a series of 156 cases of hemothorax. Nicholson and Scaddings' [2c] recent report revealed formation of a massive clot in 6 of 125 cases of uninfected and in 6 of 62 cases of infected hemothorax.

MANAGEMENT

During the treatment of the later stages of thoracic wounds in the first World War it soon became obvious that an organized uninfected hemothorax produced many of the severe and crippling deformities. Difficulty in managing this condition is best illustrated by Elliott's [6] statement: "It is paradoxically true that recovery of the chest from the crippling results of a large haemothorax may be more rapid if sepsis occurs than if the collection remains sterile." Turner [7] and Moynihan [8] recognized that removal of the foreign body from the thorax without freeing the lung and thoracic wall of adhesions was a useless procedure. These surgeons described the disability produced by an organized hemothorax and in a limited number of cases applied the principles and technic of decortication of the lung, which was first described by Fowler [9] in 1893. Since 1920 little attention has been given to the chronic type of hemothorax with the exception of Smithy's [10] revival of interest in the management of this condition.

In the treatment of chronic traumatic uninfected hemothorax, the surgical approach is governed somewhat by the site of the formation of the clot. The blood clot usually assumes a dependent position within the pleural cavity, ly-

5. Meakins, J., and Walker, T. W.: After-Effects of Wounds of the Chest, and Their Treatment, Canad. M. A. J. **8**:910 (Oct.) 1918.

6. Elliott, T. R.: Some Statistical Results of the Treatment of Chest Wounds, Lancet **2**:371 (Sept. 8) 1917.

7. Turner, G. G.: The Later Stages of Gunshot Wounds of the Chest, Surg., Gynec. & Obst. **28**:17 (Jan.) 1919.

8. Moynihan, B.: The Surgery of the Chest in Relation to Retained Projectiles, Brit. J. Surg. **7**:444 (April) 1920.

9. Fowler, G. R.: A Case of Thoracoplasty for Removal of a Large Cicatricial Fibrous Growth from the Interior of the Chest, the Result of an Old Empyema, M. Rec. **44**:838 (Dec. 30) 1893.

10. Smithy, J. G.: Traumatic Hemothorax with Special Reference to Chronic Persistent Types, J. Thoracic Surg. **12**:338 (April) 1943.

ing in the costovertebral gutter and overlying the diaphragm. Access to this region is readily accomplished by making a posterolateral incision, and the pleural cavity is entered through the seventh or eighth intercostal space. The wall of the hematoma is encountered on division of the intercostal muscles and the parietal pleura. A cleavage plane between the wall of the hematoma and the pleura may be developed with ease, owing to the fact that these structures are bound together by only a light network of vascular and fibrous tissue. The wall of the hematoma is freed from the adjacent structures by blunt dissection, working away from the thoracic wall and lung. The index finger or a blunt gauze dissector has proved satisfactory for this procedure (fig. 4). It is possible to mobilize a large hematoma in this manner without disruption of its physical characteristics (fig. 2). After the lung, the diaphragm and the thoracic wall have been freed of the hematoma, the underlying pleura may be observed to be practically normal. It is not thickened, and it still has a somewhat smooth and glistening appearance. The previously constricted diaphragm and lung will function in a normal manner with removal of the fibrous encasement. In a clotted hemothorax of less than three weeks' duration the cleavage plane between the pleura and the wall of the hematoma is not sharply demarcated. At this stage the wall of the hematoma has not become well organized and there is persistence of the edema of the adjacent pleura. Early removal of the deposit of fibrin does not permit the ready reexpansion of the lung, which is so admirably demonstrated when this structure is freed of a well organized hematoma.

The following case reports emphasize the clinical manifestations and the morbid anatomic structure of a chronic organized uninfected hemothorax. The successful application in each instance of Fowler's principles and technic of decortication of the thoracic wall, diaphragm, mediastinum and lung is described.

REPORT OF CASES

CASE 1.—A white soldier aged 19 sustained a bullet wound of the left side of the thorax on Sept. 12, 1943. The bullet entered the anterior triangle of the neck and in its course traversed the pleura, the lung and the second, third and fourth dorsal vertebrae. There was no wound of exit. He was treated for shock, and three weeks later the bullet was removed from the body of the fifth dorsal vertebra. No attempt was made to aspirate the left side of the chest until three weeks following the injury. At this time it was impossible to remove the collection of blood in the left pleural cavity. Since the date of injury, he had suffered from severe dyspnea, extreme pallor, daily low grade fever and progressive development of a deformity of the left side of the chest.

He was transferred to my service for definitive treatment. Physical examination disclosed a thin, pale, undernourished and chronically ill man. The left side of the chest was fixed, sunken and flat. Overactive respiratory excursions on the right side stood out in strong contrast to the immobility on the left. The left side of the chest had the appearance of an old empyema. The percussion note over the entire left hemithorax was flat and accompanied by an absence of breath sounds; however, in the left infraclavicular region the percussion note was hyperresonant and the breath sounds were exaggerated. On the right, physical signs of a compensatory emphysema were present. The routine laboratory tests gave negative results. A roentgenogram of the chest revealed a dense opacity involving the entire left side of the thorax with an emphysema on the right (fig. 1). Fluoroscopic examination revealed fixation of the diaphragm on the left.

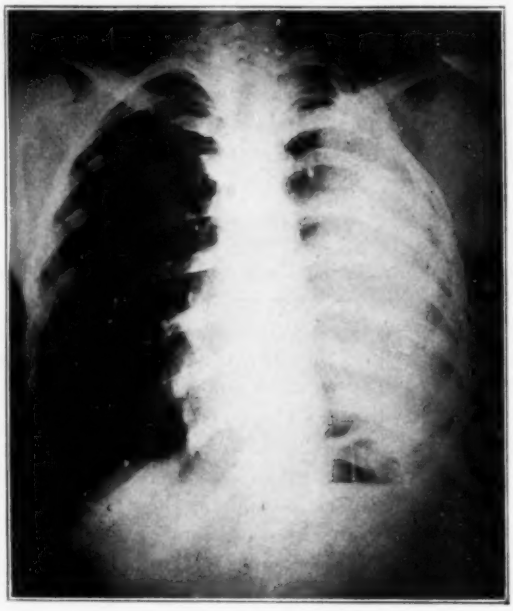

Fig. 1 (case 1).—Roentgenographic view of the thorax sixty-seven days after a gunshot wound, showing chronic organized hemothorax.

Numerous attempts to aspirate the left side of the chest were unsuccessful, and only a few cubic centimeters of a brownish fluid was obtained. This fluid failed to grow organisms on culture.

On Nov. 18, 1943, the pleural cavity was entered through a posterolateral incision. By means of an incision through the seventh intercostal space the wall of the hematoma was encountered and found to be moderately adherent to the parietal pleura. By digital manipulation the hematoma was easily separated from the parietal and visceral pleuras. It contained approximately 500 cc. of old blood, and its wall was 2 cm. in thickness. Anteriorly the hematoma terminated at the lateral border of the sternum, while posteriorly it was anchored to the aorta. It extended from the dome of the thorax to the diaphragm (fig. 2). The left lung was about the size of a grapefruit; however, neither the visceral nor the parietal pleura was thickened, and the lung readily reexpanded on completion of decortica-

tion. The left pleural cavity was drained by an intercostal tube, and the wound was closed in layers. The drainage tube was connected to an under-water seal, and 16 cm. of negative water suction was applied to hasten reexpansion of the lung.

Fig. 2 (case 1).—Gross appearance of a chronic organized hematoma.

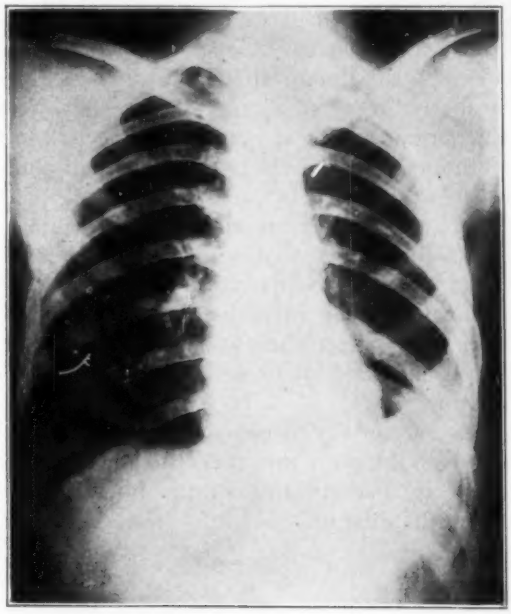

Fig. 3 (case 1).—Roentgenogram taken three weeks postoperatively. Reexpansion of the left lung is now complete.

The postoperative course was entirely uneventful. The drainage tube was removed on the first postoperative day, at which time there was complete reexpansion of the left lung. Three weeks postoperatively, there was almost a 100 per cent return of function in the left lung and the soldier was no longer dyspneic on physical exertion (fig. 3).

Case 2.—A white officer aged 32 sustained a bullet wound of the right side of the chest on Dec. 27, 1943. A bullet from a machine gun entered the right side of the chest 2 inches (5 cm.) lateral to the right border of the sternum in the fourth intercostal space. There was no wound of exit. He was given immediate treatment for shock, and no attempt was made to aspirate a hemothorax on the right side. During the ensuing five weeks he continued to have a low grade fever, lost weight, complained of a sense of constriction in the right lower portion of the chest and was dyspneic on exertion.

Physical examination at the time of his transfer for definitive treatment disclosed a moderately anemic and asthenic person. There was a scar marking the wound of entrance in the fourth intercostal space 2 inches

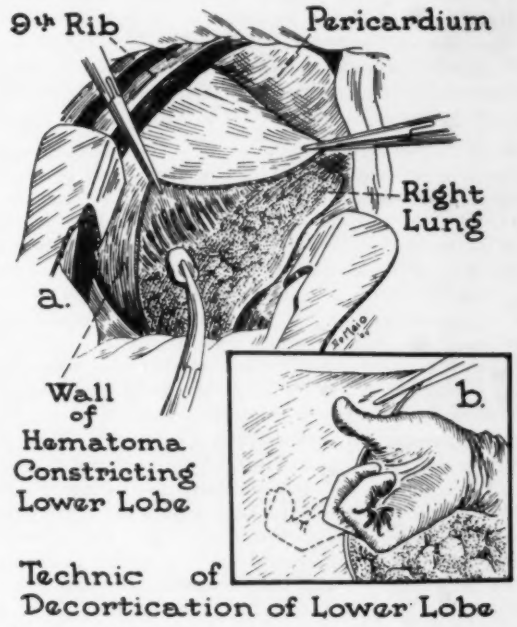

Fig. 4.—Illustrations of the operative procedure in case 2.

lateral to the right border of the sternum. He was chronically ill and dyspneic on exertion. There was a definite decrease in the respiratory excursions of the right side of the chest. The lower portion of the thoracic wall was rigid and flattened. The intercostal spaces were narrow, and the entire right side of the chest was contracted as well as limited in motion. Dulness accompanied by decreased breath sounds extended well above the angle of the scapula and high in the axilla on the right. Tactile fremitus was decreased in this region. There was compensatory emphysema on the left. The routine laboratory tests gave negative results. Roentgenologic examination revealed four foreign bodies, ranging in size from 3 by 4 mm. to 9 by 15 mm., embedded in the right side of the chest. There was diffuse haziness over the entire right lower portion of the chest, and the lower and middle lobes of the right lung were displaced toward the midline. Aspiration on numerous occasions proved unsuccessful, yielding only 5 to 10 cc. of a brownish fluid. This fluid failed to grow organisms on culture.

On Feb. 5, 1944, a right posterolateral incision was made, the right pleural cavity being entered through the eighth intercostal space. A well organized hematoma, containing approximately 700 cc. of old blood, compressed the lower and middle lobes of the lung. Removal of the contents of the hematoma did not permit reexpansion of the lung and resumption of excursions by the diaphragm. These structures were constricted and rendered immobile by the thick wall of the hematoma. The constricting walls of the organized hemothorax were removed by sharp and blunt dissection. This process of decortication permitted total and complete reexpansion of the two lobes of the lung, and the diaphragm resumed its normal function. The foreign metallic bodies, which lay in a superficial position within the lower lobe, were removed. An intercostal tube was inserted into the right pleural cavity and connected with an under-water seal. The wound was closed in layers.

The postoperative course was entirely uneventful. Clinical and roentgen examination revealed complete reexpansion of the lung on the first postoperative day. Two weeks postoperatively the patient was entirely asymptomatic and gratified with the ease of respiration. He has returned to duty.

CASE 3.—A white soldier, 32 years of age, with eighteen months of service in the army, had been entirely asymptomatic until the early part of November 1943. At this time he noticed constant and ill defined pain in the lower part of the right side of the thorax. A roentgen examination revealed a tumor mass in the posterior mediastinum extending from the level of the seventh dorsal vertebra to the level of the tenth dorsal vertebra. The tumor mass was irregular in outline but sharply demarcated. The preoperative diagnosis was ganglioneuroma of the posterior mediastinum, which was confirmed on removal of the tumor.

On November 16 a thoracotomy was performed, the right pleural cavity being entered through the seventh intercostal space. A tumor mass, measuring 10 by 6 by 5 cm., incorporated the sympathetic trunk, the greater and lesser splanchnic nerves and the seventh, eighth and ninth intercostal nerves. The overlying pleura was removed with the tumor mass. This left a considerable area in the costovertebral gutter denuded of its normal covering. The wound was closed in layers, and the pleural cavity was not drained.

His postoperative course was entirely uneventful with the exception of accumulation of blood in the right pleural cavity, which could not be evacuated with a no. 16 aspirating needle. Thoracentesis was carried out on the first postoperative day and yielded only a small quantity of dark blood. Thereafter, repeated aspirations failed to yield more than 10 cc. of blood. A roentgen film of the chest revealed an accumulation of blood in the right side of the thorax lying primarily in the costovertebral gutter at the site of resection of the tumor mass. During the ensuing sixteen days repeated cultures of a small amount of fluid obtained at the time of aspiration yielded no growth. The wound had healed by primary intention; however, the patient continued to have a low grade fever.

On December 2 the right pleural cavity was entered through the primary thoracotomy wound. A hematoma, which contained 500 cc. of old blood, lay in the costovertebral gutter and compressed the upper lobe of the right lung. The walls of the hematoma were not clearly defined. The visceral and the parietal pleura were edematous and studded with shaggy collections of fibrin undergoing early organization. The upper lobe did not readily reexpand after the fibrin was removed; however, there was definite improvement in function. A no. 32 rectal tube was introduced through the ninth intercostal space and led well up to the apex of the thoracic cavity on the right side. The tube was then connected to an under-water seal. The wound was closed in layers. Reexpansion of the right lung was complete on the first postoperative day, and the intercostal tube drain was removed. Convalescence was uneventful. In three days the temperature was normal, and there was no further accumulation of blood in the right side of the thoracic cavity. Two weeks postoperatively a roentgenogram of the chest showed the right pleural cavity to be free of pleural exudate. This soldier was returned to duty.

SUMMARY

The apparent successful treatment of acute traumatic hemothorax does not always prevent varying degrees of later respiratory disability. Temporary persistence of pain in the chest associated with mild degrees of dyspnea is not an uncommon sequela. These symptoms have been ascribed to the organization of fibrin within the pleural cavity.

The organization of a large uninfected solid hemothorax leads to serious respiratory disability and deformity of the chest. This disability coupled with futile attempts at rehabilitation demands the institution of some measure to strike patients with this complication from the role of semi-invalidism or invalidism. Application of the principles and technic of decortication of the involved anatomic structures seems to fulfil this requirement.

Cases of chronic organized hemothorax are cited which illustrate the successful surgical management by decortication of the lung, thoracic wall and diaphragm.

SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

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If slipping of the upper femoral epiphysis or epiphysiolysis is recognized at an early stage and proper treatment is instituted, the prognosis should be excellent. If it is not recognized until considerable displacement has occurred, it may produce severe crippling, whatever treatment is followed. It is the purpose of this paper to stimulate early recognition of the condition and to report experiences with various methods of treatment.

This report includes 26 patients with slipping of the upper femoral epiphysis in 36 hips.[1] They represent the total number of patients admitted to the Children's Hospital, Boston, in the last thirteen years with certain additions.[1a]

The result in 28 of the 36 hips has been evaluated after an average interval of six and three-tenths years. Of the remainder, 6 have been treated too recently for evaluation and 2 were not treated. All but 5 were examined in 1944, and the present status of all but 2 hips in the series is known. Roentgen study accompanied clinical examination in all instances.

MECHANISM AND RELATED FACTORS

The process depends on a weakening of the connection between the head and neck of the femur at the metaphysis, with subsequent displacement of the head on the neck. The neck of the femur on weight bearing tends to ride upward and anteriorly, with increasing external rotation. The head in turn tends to migrate posterior and inferior to its usual position (fig. 9 *A* and *B*). Displacement may be of any degree, from an undetectable amount to complete displacement. Owing to the natural direction of the neck of the femur, external rotation is the essential factor in the displacement.

If the slipping is of any degree the blood vessels on the anterior and the lateral surface of the neck are interrupted. The circulation to the head of the femur must then come by way of the ligamentum teres, a route which is variable and undependable, and by way of the vessels on the inferior-posterior aspect of the neck, particularly by way of those in the retinacula of Weitbrecht (fig. 9 *A* and *B*). With displacement of the head posteriorly and downward the latter vessels are shortened, as is the periosteum. Since the slipping is usually a gradual and repeated process, this shortening becomes fixed, with secondary fibrosis and formation of osteoid, which becomes calcified. Therapeutic measures designed to correct the deformity may interrupt this essential circulation, producing aseptic necrosis of the head, not only by tearing or cutting the retinacular vessels but by strangulating them through tension.

Although the cause of slipped epiphysis is unknown, certain related facts should be emphasized. It occurs at a particular period in development, most frequently between the ages of 10 and 15 years, and in the collected cases the average age of boys is 2 years older than that of girls. This reflects approximately the increased degree of skeletal maturation of the female. The process occurs at a time of rapid growth. The children affected are usually obese or large. Nineteen of the children in this series were extremely obese to obese, 6 were large but not fat and 1 was of average build. The condition is frequently bilateral, and in 10 of my patients both hips were affected. Two of the 26 patients had a sibling with the same condition.

Trauma is often described as an etiologic factor. In this series there was a history of trauma of significant degree preceding the first symptom for 5 patients. For 21 there was no known antecedent trauma, although for several

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Read in the Section on Orthopedic Surgery at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Sex: 15 boys; 11 girls. Bilateral involvement: 10 (7 males); 6 had bilateral lesions on their first admission to the hospital. Unilateral involvement: 16. Average interval between initial symptoms on the two sides: fourteen months. Longest interval between initial symptoms on the two sides: thirty-three months. Side: right 17; left 19. Girls' average age: 10 8/12 years; youngest 7 years; oldest 12 5/12 years. Boys' average age: 11 years; youngest 7 5/12 years; oldest 13 3/12 years. Average duration of symptoms on admission: 5 months.

1a. Patients treated at the Peter Bent Brigham Hospital by me are included.

of the latter trauma did precipitate the acute symptoms.

Certain comments may be made regarding these factors. It would appear that trauma has the role of provoking displacement in an antecedent condition. This is suggested by the frequency with which the condition is bilateral as well as by the history. The high frequency of bilateral disease would indicate a fundamental predisposition in the person affected, and in this the familial incidence is probably significant. The fact that many of the patients are of the so-called fat "endocrine type" may mean that there is an unknown endocrine factor, or it may merely represent the increased stress which the added weight induces. A shearing stress peculiar to the metaphysis of the femur exists, and this is increased by genu valgum, which is common in these patients.

The integrity of the connection of any epiphysis to the shaft depends largely on the binding effect of the periosteum. It is possible that with the rapid growth and the changes in the character of the periosteum which occur at this age, the periosteum loses its firm binding character [2] and allows the displacement. Howorth [3] emphasized that synovitis exists before the slipping occurs, but whether this is primary or secondary is unknown. An abnormality in the evolution of the vascular supply to the area at this particular age may be responsible, but this again has not been proved.

It is suggested, however, that there is more to the process than simply displacement of the head on the neck. In 1 of the patients in this series, for example, there was complete degeneration of the opposite joint without any recognizable slipping of the epiphysis or other discernible cause.

CLINICAL PICTURE

A child of the age peculiar to this disease, usually obese or large, acquires an antalgic hip limp, which may be intermittent or constant. All but 1 of my patients had a primary complaint of limp. Pain, though not mentioned by 5 of the patients, is usual. Activity increases the symptoms. The pain may be in the hip or groin, the anterior or anterolateral portion of the thigh or the knee. It may be present in any one of these areas or in any combination of them.

Two patients in this series who complained solely of pain in the knee had their knees examined, including the taking of roentgenograms, with no attention paid to their hips. One of these patients was sent home and two days later while walking across the floor had complete displacement of the epiphysis. It was not unusual for the patients in this series to have had previous medical observation over a relatively long period without the condition being recognized.

Even when the symptoms are mild, physical examination will usually disclose limitation of internal rotation, flexion and abduction of the involved hip with pain and muscular spasm on the extremes of these motions. Hyperextension of the hip may be increased. Limited internal rotation is usually the earliest suggestive physical finding. Often the hip tends to go into external rotation as it is flexed.

As the process increases the limp and pain increase. The gait may be frankly waddling if the involvement is bilateral. Spasm may be present on all motions. A fixed external rotation deformity may develop. It was present in 50 per cent of the patients in this series.

If acute displacement occurs, the signs are those of a fractured neck of the femur with extreme muscular spasm, the extremity being in external rotation.

Frequently there is a history of minor discomfort for some weeks or months, followed by relatively mild trauma, which precipitates the acute symptoms.

ROENTGEN EXAMINATION

Careful roentgen examination of the hips, including the taking of lateral projections, is essential. The lateral films are best taken in the frog position, that is with the hip externally rotated. The earliest findings are rarefaction of the neck adjacent to the epiphysial line and minimal displacement of the neck anteriorly on the head (fig. 3 *A* and *B*). The latter can be seen only in the lateral projection. The films must be of excellent quality before a report of negative results is given, if the history and physical signs are suggestive; in fact, in such cases the patient should be carefully observed and the roentgen examination repeated after a short interval.

If there is much displacement the condition is recognized easily in both the anterior and the lateral projection. If the slipping is of some duration, irregular callus may be seen filling in the angles between the head and the neck. At this stage the picture in the neck may be one of mottled density and rarefaction.

If slipped epiphysis exists it should be considered an emergency, since at any time marked

2. Key, J. A.: Epiphyseal Coxa Vara, J. Bone & Joint Surg. **8**:53-117, 1926.

3. Howorth, M. B.: Slipping of the Upper Femoral Epiphysis, Surg., Gynec. & Obst. **73**:723-732, 1941.

increase in the displacement may occur. If it does the prognosis is greatly impaired.

TREATMENT AND RESULTS

In considering the results of treatment for slipped epiphysis it should be emphasized that individual cases are not directly comparable, whether owing to variations in the degree of displacement, duration of the disturbance or other factors. What might be a good result in 1 patient, based on the original condition, might be a poor result in another.

The results in this paper are evaluated not on the basis of improvement from the original condition but on the basis of normal painless function. Using the normal hip as a standard was not satisfactory, since in many of the patients the process was bilateral. In order to express the amount of motion in the hips by a single composite figure the coefficient proposed by Ferguson and Howorth,[4] in which 90 to 110 is estimated as normal, has been used.

The various methods of treatment used in this series may be classified as follows: (1) closed reduction with spica fixation; (2) traction-spica-traction method without manipulation; (3) skeletal fixation in situ (without arthrotomy) for those hips with minimal displacement; (4) open reduction with skeletal fixation for those hips with pronounced displacement; (5) miscellaneous methods, including traction, non-weight-bearing brace, crutches, etc. (reported in table 1).

4. Ferguson, A. B., and Howorth, M. B.: Slipping of the Upper Femoral Epiphysis: Study of Seventy Cases, J. A. M. A. **97**:1867-1872 (Dec. 19) 1931.

Closed Manipulation with the Patient Under Anesthesia with Spica Fixation.—Three patients in this series were treated by this method, and the results have been evaluated after an average of ten and three-tenths years (table 1).

My interest in slipping of the upper femoral epiphysis originated from contact with a patient who had closed reduction of a severely displaced upper femoral epiphysis. Her history follows.

J. M., a girl of 11 years, was seen at the Children's Hospital on June 27, 1931, with the complaint of severe pain in the left hip following a fall one hour before. She had had mild pain in this hip and limp for six weeks preceding the fall, which were said to have followed bending exercises in school. They had recurred with exercises and were relieved by rest. The family and the past history were irrelevant except for the fact that the family was generally obese and that the child herself had been treated for knock knees.

TABLE 1.—*Results of Miscellaneous Treatment*

Patient	Years Followed	Estimated Original Displacement, Cm.	Treatment	Index of Motion (Ferguson-Howorth)	Pain	Significant Deformity	Arthritic Change	Shortening	Limp	Result
A. C.	12½	1.5	Thomas brace with patten	87.8	0	++	0	Bilateral	0	Good — Other side slipped while brace was being worn
	12	1.5	Thomas brace with patten	87.2	0	++	0	Bilateral	0	Good —
M. H.	6	0.8	Traction, 4½ mo.; Thomas brace with patten and crutches, 4½ mo.	106.5	0	0	0	2 cm.	0	Excellent
B. S.	3	1.3	Traction, 5 mo.; crutches	70.3	0	++	?	Bilateral	0	Good —
		1.5	Traction, 5 mo.; crutches	56.3	Occasional	Severe	Cup	Bilateral	++++	Poor. Seen first 7 and 14 months after onset; severe degenerative changes on admission
J. M.	13	Severe	Manipulation and spica	52	0	++++	+++	4 cm.	+	Poor; aseptic necrosis; other hip stiff without slipping
E. L.	10	Severe	Manipulation and spica	61.5	0	++ ?	0	Bilateral	0	Fair
	9	?	Manipulation and spica	49.5	0	+++	0	Bilateral	++	Poor +

Physical examination: Examination showed an extremely obese girl, whose physical findings were essentially within normal limits except for the left hip. The extremity lay in extreme external rotation, and any attempt at motion provoked severe muscular spasm and pain. Roentgenograms showed pronounced displacement of the head on the neck, the shadow of the neck being superimposed on the lateral margin of the acetabulum (fig. 1 *A*).

Treatment: Within twenty-four hours the hip was manipulated with the patient under anesthesia, into what was interpreted roentgenologically as a good position. A spica held the hip in internal rotation and abduction. When the plaster spica was bivalved at the end of three months, the head showed increased density and definite evidence of aseptic necrosis (fig. 1 *B*). The extremity was placed in counterpoised traction for several months. The increased absorption of the neck and head may be seen in roentgenograms which were taken on Feb. 11, 1932 (fig. 1 *C*), but the head did unite to the neck.

During this period there was progressive loss in the motions of the opposite hip joint, and the joint space became thinner, although there was no evidence of

slipping of this epiphysis or other causative disease. The condition of the two joints may be seen in the roentgenogram taken on June 31, 1933 (fig. 1 *D*). The head on the left has been revascularized and united to the neck, although it is extremely deformed. The narrow joint space may be seen on the right, with definite irregularity in the contour of the head.

The last examination, on May 17, 1944, almost thirteen years after the original manipulation, found her to be no longer obese. The right hip, the one in which demonstrable slipping did not occur, showed only a jog of motion. The left hip showed flexion of 60 degrees, and external and internal rotation of 35 degrees in extension with abduction of 20 to 25 degrees and hyperextension of 20 degrees. She was able to walk without pain. She wore a 1¼ inch (3 cm.) raise on the shoe on the side of the displaced epiphysis. Roentgenograms taken on this date showed essentially

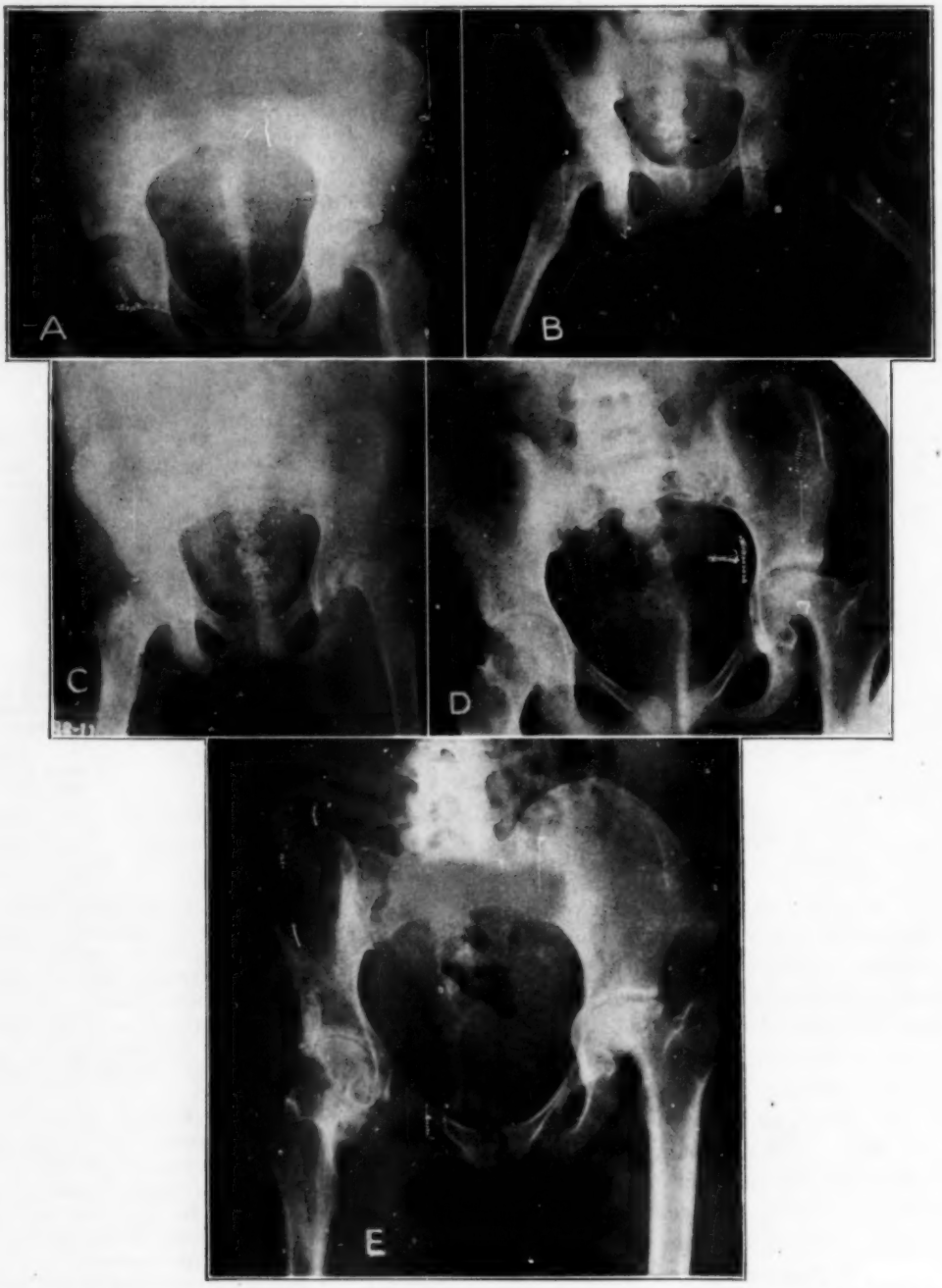

Fig. 1 (J. M.).—Treatment: closed manipulation. *A* (June 27, 1931), an anterior view shows essentially complete displacement of the head on the left side. *B* (Sept. 14, 1931), two and one-half months after closed reduction. The head is dense, and there is aseptic necrosis. *C* (Feb. 11, 1932), increased absorption of the neck and head. *D* (June 31, 1933), the distorted head is well united and revascularized; there is a good joint space. Note the narrowed joint on the right with reaction at the periphery of the head. *E* (May 17, 1944), the head on the left is about the same as eleven years before. The joint space on the right side is narrow, with distortion of the head and overgrowth of bone. There is a jog of motion only.

the same contour of the head as seen eleven years before, with distinct irregularity but with an adequate joint space (fig. 1 *E*). The right hip had an appearance which suggested the possibility of slipping of the epiphysis in the past, with decided narrowing of the joint space and formation of new bone. Serial films taken during the period when difficulty with this hip arose, however, had shown no evidence of such an occurrence. She had a shortening of 4 cm. Her result was recorded as poor.

Three hips were treated by closed reduction, with the patients under anesthesia. All 3 showed severe limitation of motion, as expressed by the coefficient used. The hip of the patient just mentioned had a coefficient of 52 (normal 90 to 110). The other 2 hips treated by this method had a coefficient of 61.5 and 49.5 (table 1). In none of the hips has there been pain up to the time of writing, but 2 have caused a definite limp.

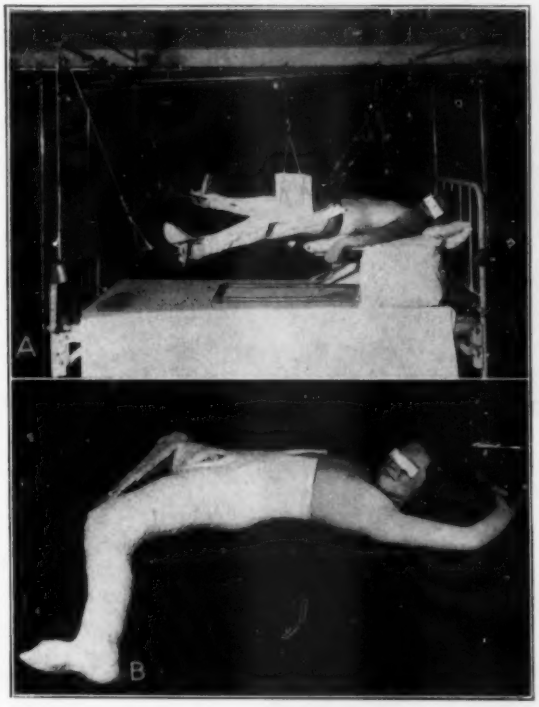

Fig. 2.—*A*, patient in traction, with the left hip involved. Note the internal rotation arm. The other hip is suspended to control the degree of abduction. *B*, patient in a spica cast, with the hip in internal rotation and abduction. The left hip is involved, and the plaster goes only to the knee on the right. The left hip is not in hyperextension as the photograph suggests.

It is anticipated in all of these hips that, judging from their roentgen appearance, further difficulty may be expected.

Traction-Spica-Traction Method.—The method takes into cognizance certain facts:

1. The blood supply to the head of the femur must not be traumatized.

2. Spasm ordinarily quiets down with traction, allowing increasing internal rotation and abduction.

3. Slipping cannot increase if the hip is immobilized in abduction and internal rotation.

4. Immobilization promotes rapid healing.

5. Immobilization in plaster with the method used has not resulted in stiff hips.

6. If the displacement is not too great, the surfaces smooth off as the process heals.

More hips were treated by this method than by any other—18 hips of 13 patients. This treatment was first used thirteen years ago. Patients ascribed as having been treated by the traction-spica-traction method followed a variation of the following routine.

Two traction forces are applied to the involved extremity: one longitudinally and the other to develop internal rotation (fig. 2 *A*). In practice longitudinal traction is applied through moleskin adhesive tape straps to the thigh and leg; internal rotation is accomplished by applying a wide moleskin adhesive tape strap around the thigh. This wide strap starts on the anterolateral aspect of the thigh and passes around the medial aspect of the thigh, beneath the posterior surface and up the lateral aspect. From the junction of the posteromedial aspect on, it is faced with felt, so that it will not stick to the inferior aspect of the thigh. Overhead traction is applied to the free end. Only moderate traction is used longitudinally, usually somewhere between 5 and 10 pounds (2.3 and 4.5 Kg.), and the amount applied to the internal traction arm is evaluated as the traction is observed. Usually 5 pounds is used at the start; internal rotation must not be forced. The leg may be suspended in a Thomas splint, suspended by balanced slings or kept flat on the bed, as in Buck's extension, with the added arm for internal rotation. Traction is started in a neutral position; abduction and internal rotation are increased as tolerated comfortably. There should be no pain; the patient should be more comfortable rather than less. Traction must be started in the line of deformity. In practice the opposite leg is placed in traction and suspension so that the degree of abduction and rotation can be controlled.

As soon as spasm is relieved and the maximal degree of internal rotation and abduction obtained, the patient is placed in a hip spica (fig. 2 *B*). Traction is used on the average for three weeks. The essential function of the spica is to maintain the involved hip in the maximal comfortable degree of abduction and internal rotation.

This is accomplished by extending the spica to the knee on the uninvolved side and including the foot on the involved side with the knee in moderate flexion. The hip should be in slight flexion and never hyperextended. Ordinarily the patient is sent home in the spica and is readmitted to the hospital after three months. At this time the spica is removed and the condition of the epiphysial line is evaluated by roentgenograms; ordinarily there is appreciable healing at this stage.

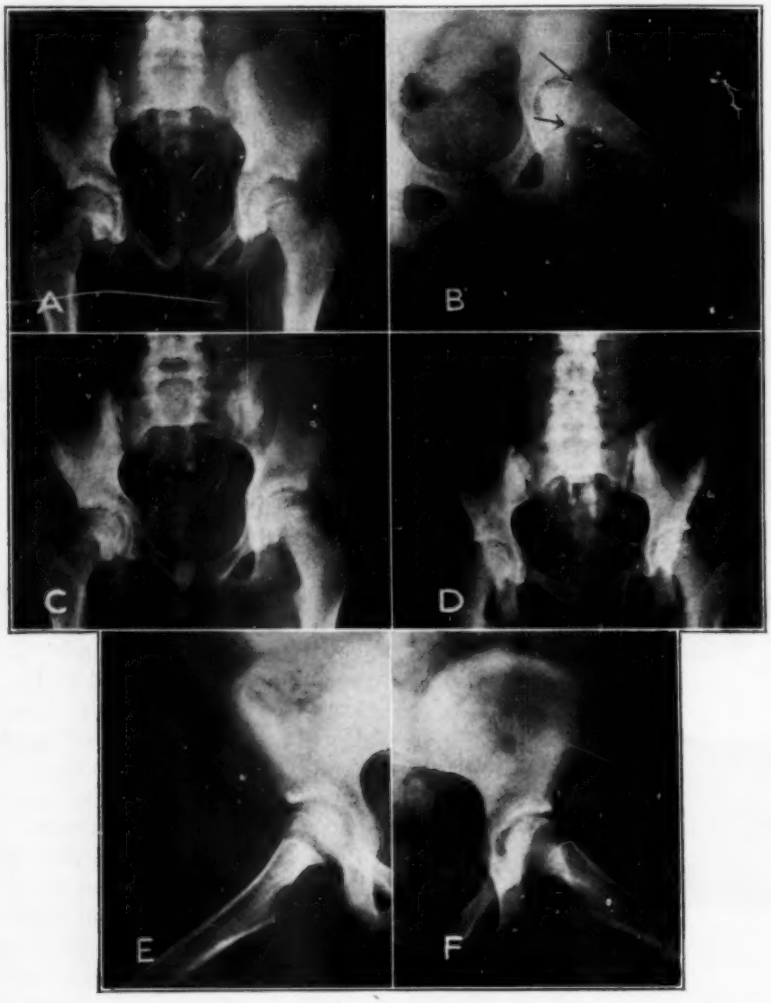

Fig. 3.—R. V., a girl 10 years of age, who had a limp on the left side for ten weeks. Treatment: traction-spica-traction. *A* (Sept. 5, 1941), an anterior view shows rarefaction in the metaphysial region of the left side. *B*, the lateral projection shows 0.7 cm. of anterior displacement of the neck on the head. *C* (Dec. 1, 1941), note healing three months later. *D* (May 17, 1944), the epiphysial line is closed on the involved side on the left; the neck is a little broader on this side. *E* and *F* (May 17), lateral views of the two hips show their similarity in contour. The contour of the left hip is much better than the contour shown in *B*.

Restoration of function must be accomplished gradually. Counterpoised traction is most useful in this period. The extremity is placed in traction with a Thomas splint and a Pearson attachment and counterbalanced. The patient is encouraged to move the extremity. Under water exercises are helpful. On occasion counterbalance traction is not used, and the patient is allowed to develop motion in bed. Walking is started with crutches, not with a brace. The actual time of walking, as of all sequences with this treatment, depends on the roentgen appearance and the clinical findings.

Since the group of patients treated by this method is large and since the results are uniform, the individual cases are not presented in tabular form. A summary of the time involved in this method of therapy may be seen in table 2. The summary of results in this group of patients may be seen in table 3.

The hips treated by this technic showed a variable amount of initial displacement; the esti-

mated average was 0.8 cm., and the maximal amount was 1.5 cm.

The results in the 13 patients who had a follow-up examination after an average of six years following treatment may be classified as excellent. All patients had a normal coefficient of motion, which averaged 98.5 (90 to 110 normal) (figs. 3, 4 and 5). Flexion and abduction, motions ordinarily limited after slipped epiphysis, were normal in all, and internal rotation was normal except in 1 patient who had both hips involved; he had internal rotation of only 20 and 10 degrees respectively at his last examination, eleven years after treatment. His hips might be placed in the good category, although he considered his hips normal in all respects. He had had maximal displacement. None of the patients had pain or limp. There was an average shortening with unilateral involvement of 1 cm.

TABLE 2.—*Summary of the Time Involved with the Traction-Spica-Traction Method for Eighteen Hips of Thirteen Patients* *

Phase of Treatment	Duration
Traction; average period	3 weeks
Cast; average period	3½ months
Counterpoised traction when used	1 month
Walking with crutches; average period after initial treatment	5 months
Walking unprotected; average period after initial treatment	7½ months
Full activity; average period after initial treatment	11½ months

* In all cases in which the condition was bilateral but one the hips were treated simultaneously, i. e., the condition was bilateral when seen.

Four hips in 3 patients who were still receiving treatment at the time of writing are not included in this table.

TABLE 3.—*Results of the Traction-Spica-Traction Method in Eighteen Hips*

13 hips: average follow-up period, 6 years	
	Average original displacement: estimated 0.8 cm.; maximal, 1.5 cm.
	Coefficient of motion (Ferguson-Howorth): all normal; average 98.5 ((normal 90-110)
	Flexion and abduction: normal limits in all
	Internal rotation: normal except for 1 patient in whom internal rotation of both hips was reduced
	Pain: none
	Limp: none
	Increase in slipping: none
	Average shortening with unilateral involvement: 1 cm.
4 hips: treatment too recent for evaluation; 1 of these had	increased slipping with full activity too soon
1 hip: healing with normal motion; patient transferred to	another hospital, where hip was nailed
18	

Four hips of 3 patients in this group were treated so recently that the results could not be evaluated, but 1 of these patients should be discussed.

She was admitted at the age of 9 years and 9 months, with a two week history of pain and limp. She had minimal displacement of the head, only a few millimeters, associated with rarefaction of the neck adjacent to the epiphysis. She had the usual treatment except that she was immobilized in a spica for only two months. She started walking with crutches four months after the onset of symptoms and was soon allowed full activity. After a few months she started to limp but did not complain of pain. The clinician who observed her reduced her activity partially, but she returned later with a displacement of 1.5 cm., as estimated from the roentgenograms. This occurred recently, and the final result cannot be stated. This recurrent slipping should not have happened with proper supervision. The symptoms gave adequate warning of recurrent difficulty before increased displacement occurred.

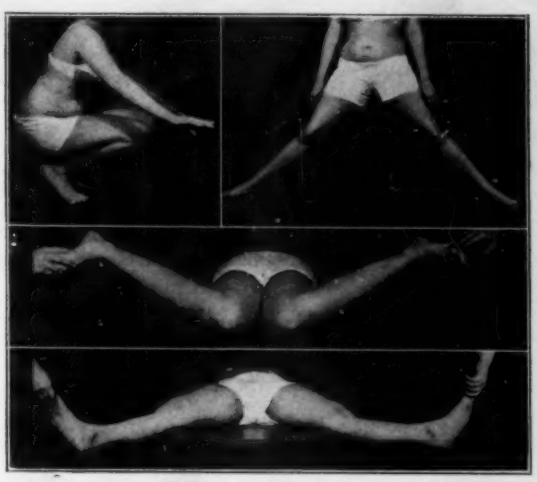

Fig. 4.—Photographs of R. V., taken on May 17, 1944, two years and eight months after slipping, show full range of action in the motions often limited after slipped epiphysis.

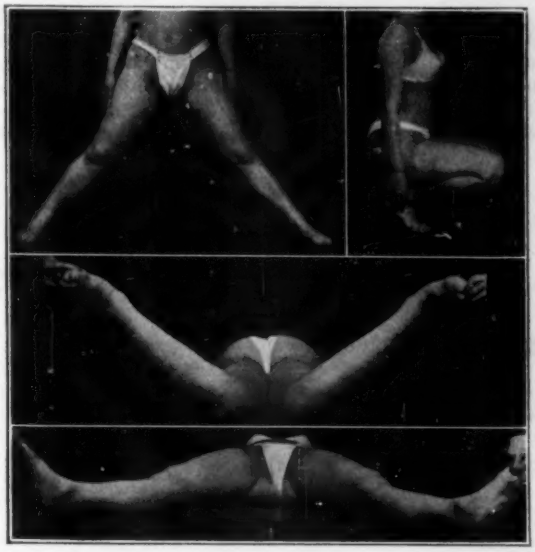

Fig. 5.—E. C. had slipped epiphysis on the right side seven years before, with so-called minimal displacement. The traction-spica-traction method was the treatment employed. Normal motion resulted, with no residua.

There has been no increase in the slipping in the other hips of the patients of this group, either during treatment or afterward. Instead

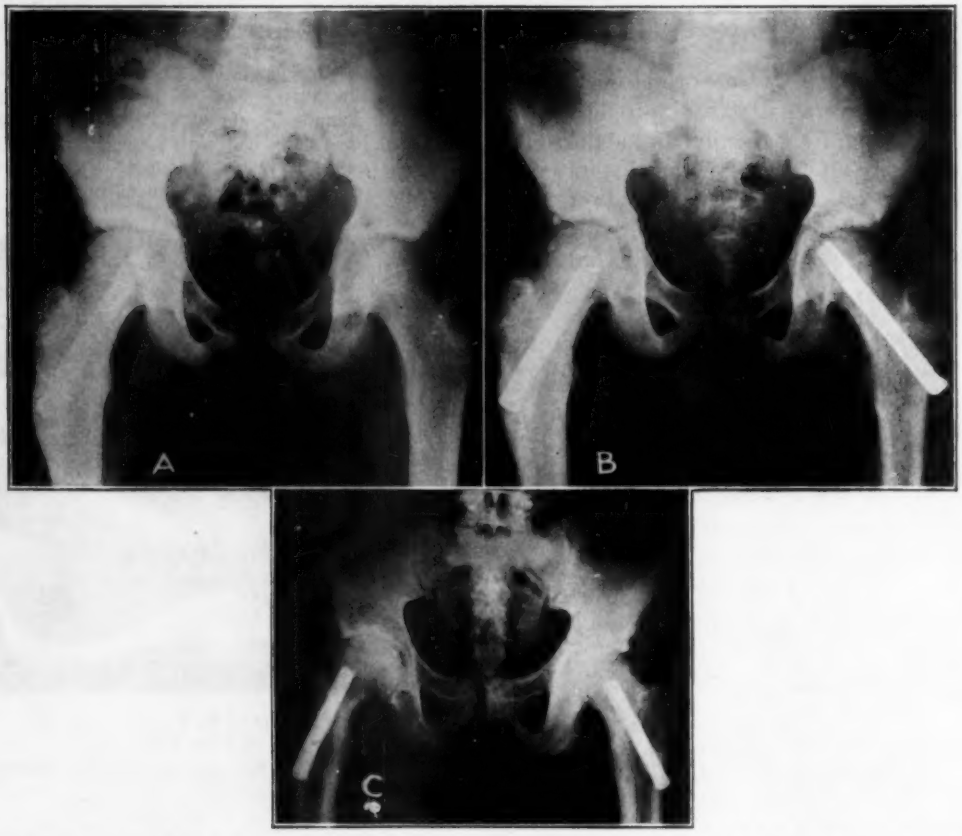

Fig. 6 (R. B.).—Minimal slipping on the right at 12 years of age and on the left one year later. Treatment: nailing in situ. *A*, eight months after the right side was nailed. Note position of the nail across the epiphysial line. The nail is in a good position in the lateral view. *B*, six months later, after the other side was nailed. The nail is deep in position. *C*, note position of the ends of the nails five years later. Neither nail reaches the site of the closed epiphysial lines. This is due to growth of the neck. The changed angle of the nail on the right indicates farther slipping. This was confirmed in the lateral view.

TABLE 4.—*Results of Nailing in Situ and Open Reduction with Nailing*

Patient	Years Followed	Estimated Original Displacement	Index of Motion	Pain	Significant Deformity	Arthritic Change	Shortening	Limp	Result
					Nailing in Situ				
A. B.	6	0.4 cm.	80.5	Rare +?	+	0	Bilateral	0	Good —
	5	0.2 cm.	84.5	0	0	0	Bilateral	0	Good
A. C.	2½	0.3 cm.	98.5	0	0	0	1.0 cm.	0	Excellent
G. N.	1¼	0.5 cm.	90.0	0	0	0	0.6 cm.	0	Good +. Nailed elsewhere; at time of writing other hip was involved
R. S.	5 mo.	0.3 cm.	....	..	..	..	.....	..	Too early to evaluate
					Open Reduction with Nailing				
R. B.	5½	Severe for months	23	Occasional +++	++++	Cup	2.0 cm.	+++	Poor; aseptic necrosis
D. B.	7½	Acute, complete	91.5	Rare +?	++	+?	0.7 cm.	0	Good ?
D. P.	1¼	Acute, complete	100.5	0	0	0	0.6 cm.	0	Excellent
Ro. B.	6 mo.	Severe for months	93.0	..	..	..	.....	..	Too recent to evaluate; apparently excellent

the contours have improved with the healing phase (fig. 3 *B* and *F*).

The final hip in this group of patients which could not be evaluated was healing with excellent motion when the patient was transferred to another clinic for outpatient observation, since he was over age for the Children's Hospital. This hip was nailed after he was transferred, for the sole reason that the epiphysial line was not completely closed.

Nailing in Situ.—Five hips with minimal displacement were treated in this manner. In each instance a large Kirschner wire was inserted as a guide and a cannulated modified Smith-Petersen nail was introduced through a lateral incision without arthrotomy. In all cases the nail was in a good position.

Fig. 7.—A. C., a boy of 14 years with pain and limp on the right side for five months. Treatment: lateral nailing in situ without arthrotomy. *A* (Nov. 10, 1941), an anteroposterior view shows changes in the neck adjacent to the epiphysis. *B* (November 10), a semilateral view shows an anterior displacement of the neck of about 4 mm. *C* (May 6, 1942), six months after nailing: The nail is in position. The epiphysial line is narrower on the right. *D* (May 3, 1942), two and one-half years after nailing: The nail was removed when the line had become obliterated, ten months after nailing. The neck is broader than normal. The line of the nail is still visible.

The results in the 4 hips which were evaluated after an average of four and eight-tenths years following the nailing were good (the fifth hip was nailed too recently for evaluation), but neither in the contour of the hips nor in motion were they as good as those after treatment with the traction-spica-traction method (table 4). Two hips (of 1 patient) had a coefficient of motion below 90, namely 80.5 and 84.5. In 1 of these hips, which was fixed with the nail in excellent position deep in the head, an increase in displacement of the head on the neck developed subsequently (fig. 6). This arose not from a change in the position of the nail but from growth of the neck, by which the nail was retracted from the head across the epiphysial line. This patient has on rare occasions minimal discomfort in the upper lateral part of the thigh on the involved side, but this may arise from the nail, which should be removed. The average coefficient of motion for the 4 hips was 88.4, which is just below the ascribed limit of normal, or 90. The results in the patients in this group were characterized respectively as excellent, good + good and good — (figs. 7 and 8).

Open Reduction with Skeletal Fixation.—Four hips were treated by open reduction with nailing; in all the displacement was severe (table 4). The results in the patients of this group were determined after an average of four and eight-tenths years. In 2 the original displacement was acute and essentially complete; in the other 2 the displacement was of several months' duration. In 1 patient, R. B., aseptic necrosis developed postoperatively and the result was poor. The second patient in this group, D. B., although her hip had a normal coefficient of motion and may be described as good at the time of writing, had after operation some changes in the head of the femur, which now has minimal irregularity in contour.

The last 2 patients in the open reduction group, D. P. and R. B., had reduction of the dis-

placement with a variation in technic, which I believe is important. In these patients, the circulation of the head was perfectly maintained. One of the hips, which has been observed sufficiently long to evaluate, has normal function in all respects; the other, although it is too soon to assess the result, has excellent function at the time of writing.

The operation as performed recognizes the importance of the posteroinferior cervical vessels particularly the vessels in the retinacula of Weitbrecht, in maintaining the circulation of the head and the importance not only of not cutting them but of not stretching them so as to interfere with their lumens. It recognizes, as pointed out elsewhere, that since the head in slipped epiphysis has usually been in a posterior-inferior position for some time, with resultant shortening of these

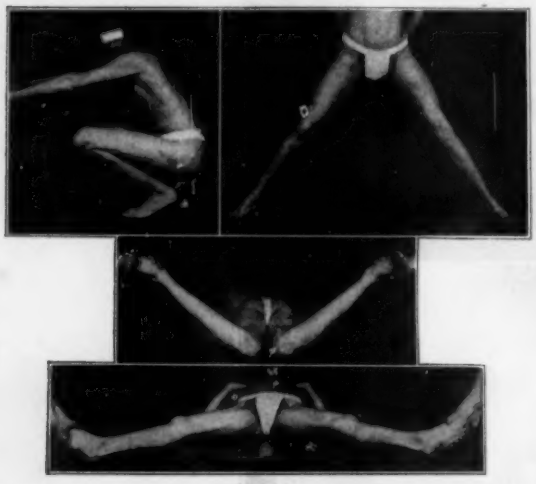

Fig. 8.—Clinical photographs of A. C. taken in June 1944, showing excellent range in motions frequently limited in slipped epiphysis. Rating: excellent.

vessels and the surrounding soft tissues, reduction of the head by prying it into position compromises the blood supply to the head from this source (fig. 9*A* and *B*).

The operation has the following essential features. On exposure of the neck of the femur, a longitudinal incision is made in the periosteum on the anterior aspect of the neck with a transverse prolongation over the anterior and lateral aspect of the proximal end of the neck. The periosteum is carefully stripped from the neck with a curved elevator, with preservation of the periosteum and retinacula on the inferior-posterior aspect (fig. 9*C*).

At this stage, if the displacement is fresh, the soft osteoid may be separated with little effort and the proximal end of the neck exposed. If the connection is more firm, separation is accomplished with an osteotome and a hammer. In the healing phase, this bone may be hard. The periosteum and the retinacula on the posteroinferior aspect must not be cut or traumatized.

Once the neck has been cut across, a sufficient section of the neck is removed to allow the head to be placed in position without stretching or twisting the periosteum and the retinacula (fig. 9*D* and *E*). The shape of the section removed varies with the deformity and should be designed to restore the normal angle of the neck and the head. If the slipping is recent, the line of the osteotomy is essentially parallel to the "fractured surface" of the neck. If the slipping is of some

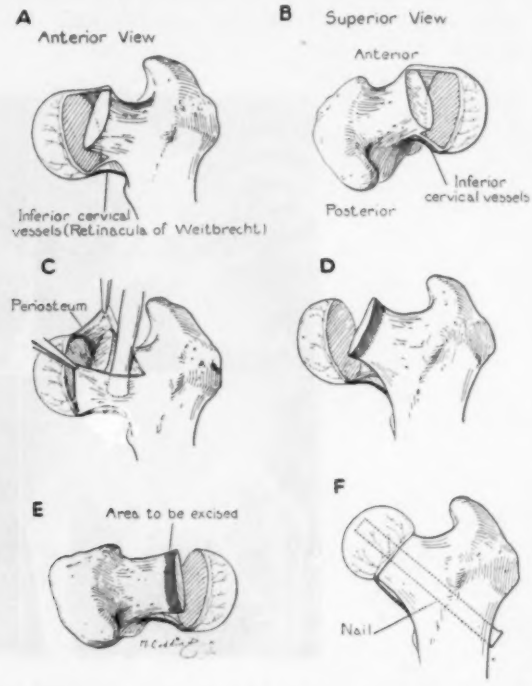

Fig. 9.—Diagrammatic drawings. *A* and *B*, anterior and superior view respectively of the head and neck of the femur in slipped epiphysis, showing the direction of displacement of the head. The neck rotates laterally and comes to occupy a superior and anterior position, and the head comes to occupy an inferior and posterior position. The apparent space between the head and neck does not exist. The inferior cervical vessels in the retinacula of Weitbrecht may be seen supplying the head. *C*, the periosteum is being elevated, to protect the retinacular vessels. *D* and *E*, diagram showing bone to be excised from the neck to allow replacement of the head without tension on the retinacular vessels. The amount of bone excised varies with the condition. *F*, the head is replaced with skeletal fixation; the vessels are intact.

duration and there is formation of new bone, it is necessary to remove more bone superiorly and anteriorly. The head is then fixed in position in the usual manner, with skeletal fixation (fig. 9*F*). If the process is healed at the time

of osteotomy, there is no reason why osteotomy may not be done, a little way removed from the site of the epiphysial line. This makes fixation more simple, but the osteotomy should not be done too far distally, for it will interfere with the circulation of the head.

Fig. 10 (D. P.).—Treatment: open reduction with nailing. *A* (March 27, 1943), anteroposterior view shows complete displacement on the left. *B* (May 20, 1944), the bone is well united with the nail in position. *C* (May 20), a lateral view shows excellent contour.

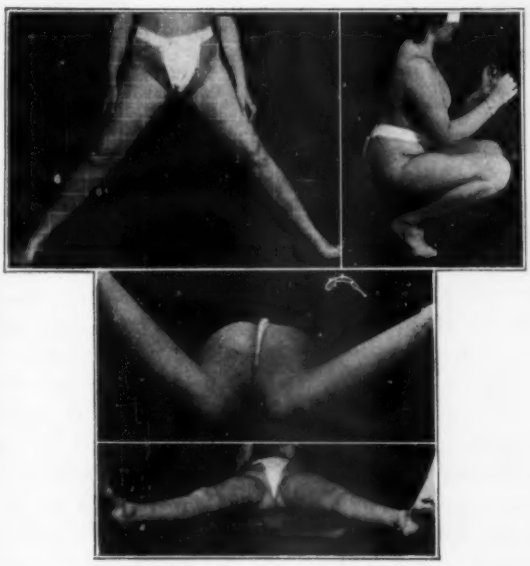

Fig. 11.—Clinical photographs of D. P. taken one year after operation. Motion is normal.

The hips treated by this method have a coefficient of motion of 100.5 and 93.0. The history of 1 of the patients in this group is included.

D. P., a girl aged 11 years and 10 months, was admitted to the hospital on March 29, 1943, complaining of extreme pain in the left hip following a fall. She had had some discomfort in this hip eight months before, but this had subsided.

Physical Examination: Examination revealed an obese girl in obvious pain; the hip was held in external rotation of 45 degrees, with severe muscular spasm and pain on any motion. Roentgenograms showed essentially complete displacement of the head on the neck (fig. 10 *A*).

Treatment: The day after her admission to the hospital, operation was performed, with resection of enough of the proximal neck of the femur to allow reduction without stress on the retinacular vessels. Fixation was accomplished with a nail. Postoperatively the patient was kept in traction for six weeks, with increasing motion. She was not allowed to walk with partial weight bearing using crutches until June 15, and only after six months following the operation was she allowed activity without crutches.

Follow-Up Examination: One year and two months later examination disclosed painless function, normal in all respects (fig. 11). Roentgen examination on May 20, 1944 showed the nail in position and good contour of the hip (fig. 10 *B* and *C*).

COMMENT ON TREATMENT

The final evaluation of the results of treatment in this disease depends on the lifetime experience of the patient. The head of the femur is so peculiarly subject to degenerative changes in late adult life that what may appear to be a good hip at 25 years of age has the possibility of acquiring secondary changes which would place it in the poor category at a later age. A study of fifty-year end results would give the answer.

The best results were obtained with the traction-spica-traction method and the next best

results with the nailing in situ method without arthrotomy. The results in these two groups were comparable except for the paucity of patients whose hips were nailed. However, the results which I obtained with nailing in situ were essentially the same as those reported by Klein, Joplin and Reidy [5] in a larger number of patients treated by this method.

In this series the hips nailed in situ had less average initial displacement than those treated by the traction-spica-traction method, 0.4 compared with 0.8 cm.

In the follow-up study the average coefficient of motion in those hips treated by the traction-spica-traction method was 98.5; that in those nailed was 88.4. The only patient in the two groups who had discomfort referable to the hips was 1 whose hip had been nailed. This was probably due to the head of the nail. The nail had not been removed.

The evidence would suggest that either the traction-spica-traction method or the nailing in situ method is satisfactory for slipped epiphysis with minimal displacement and that in addition the traction-spica-traction method is effective for those hips with moderate displacement up to an estimated amount of 1.5 cm.

Proponents of the nailing method would point out that with this method the stay in the hospital is short, the time that the patient must be protected is brief and there is no worry about further slipping. The disease, however, is frequently bilateral, and after nailing followed by full activity involvement of the other side is common. In 2 of the 5 hips in this series which were treated by nailing in situ and in 3 of the 11 reported by Klein and co-workers, slipping occurred on the opposite side after nailing. Furthermore, in 1 of the hips which was well nailed according to all criteria, further slipping occurred, despite the presence of a nail. This arose from growth of the neck, which carried the nail distally across the epiphysial line. The result in another hip treated by this method corroborated the fact that growth may occur with the nail extending across the epiphysial line, as shown in certain experimental work.[6]

The advantage of the traction-spica-traction method is that the results so far seem to be better than those obtained by other methods. The contention that further slipping may occur with the hip in traction and that stiffness is induced by fixation in a plaster spica is not validated by my experience.[7] Further displacement cannot occur if internal rotation is maintained.

Criticisms of the method are that it requires longer care and hospitalization, that the disability during the treatment phase is long and that the possibility of recurrent slipping exists until the epiphysial line is obliterated. In practice the line heals prematurely after slipping, and it has in most instances healed promptly after treatment. Once the healing phase is reached, further progress of the process can be accurately evaluated by history, clinical signs and roentgenography.

In only 1 of 18 hips which were treated by the spica-traction-spica method was there recurrent slipping. Recurrence occurred after a brief period of immobilization while the patient, under 10 years of age, was observing full activity. The clinician had adequate warning of difficulty, as evidenced by a recurrent limp some time before the slipping occurred. This patient, though the process is too recent to evaluate, gives every indication that a good result will be obtained despite the recurrence of slipping.

Increased slipping has not occurred in the other hips for which this method was used. It has been found instead that the contour improves, probably not by any reduction of the displacement of the head but rather through growth and adaptive factors.

The limited activity which patients in this group need to follow for a period is probably helpful in preventing involvement of the second side. In only 1 instance did slipped epiphysis occur on the opposite side after treatment by this method, and this was nearly three years after the initial side was affected.

In an attempt to decide whether a hip shall be treated by nailing or by the traction-spica-traction method many considerations arise. Three of these factors may be listed: the facilities available for therapy; the experience of the personnel who will carry on the treatment, and the effectiveness with which the activities of the patient can be controlled. Treatment by the traction-spica-traction method demands effective control, but in this group of patients there was little difficulty on this score, although most of them were from the public ward. Certainly harm can occur in the nailing of hips by men who are not properly prepared to perform the procedure. On the other hand, the traction-spica-traction method must be handled properly too. One patient in this group,

5. Klein, A.; Joplin, R. J., and Reidy, J. A.: Treatment in Cases of Slipped Capital Femoral Epiphysis at the Massachusetts Hospital, Arch. Surg. **46**:681-686 (May) 1943.

6. Green, W. T., and Harris, L.: Unpublished data.

7. Mayer, L.: The Importance of Early Diagnosis in the Treatment of Slipping Femoral Epiphysis, J. Bone & Joint Surg. **19**:1046-1051, 1937. Wilson, P. D.: Treatment of Slipping of the Upper Femoral Epiphysis with Minimal Displacement, ibid. **20**:379-399, 1938.

for example, had slightly increased hyperextension of the knee on the involved side, which arose from faulty application of a plaster spica.

The final criterion in choosing between the methods will depend on how the hips stand up in the future. Is the better function of the hips which have been treated by the traction-spica-traction method pertinent to their future progress? Is the slightly lessened function of the hips which have been nailed significant? Certainly the hips nailed are good at the time, but the question arises as to whether they will be as good in the future.

It is possible that the results obtained from nailing in situ might be improved by preliminary traction if there is any degree of spasm, by skeletal fixation using a less traumatic method and by protecting the hip longer in the postoperative period.

For patients with extreme acute displacement the indication for open reduction with skeletal fixation seems real. Although my experience is too limited for conclusions to be drawn, it would seem that preservation of the retinacular vessels and excision of enough of the neck to allow replacement without strangulation of these vessels should obviate or at least greatly decrease the incidence of aseptic necrosis of the head of the femur.

The same technic applied to a hip which has healed with extreme displacement gives promise of being equally good, although the technical difficulties are much greater in this stage.

Unanswered is the question as to just how much displacement warrants an open procedure. One patient with the heads equally displaced to an amount estimated as 1.5 cm. had excellent function eleven years after treatment with the traction-spica-traction method. Whether it will be good after fifty years is the question. At the present time any displacement over 1.5 cm. is considered as warranting an open procedure. This is subject to revision, however.

My experience with closed reduction may be added to other evidence against this method. With such a manipulation there is a likely possibility of interrupting the retinacular vessels and producing aseptic necrosis. This does not mean that on occasion with acute displacement gentle reduction may not produce a good hip.

The use of a walking brace for 1 of the patients was followed by slipping on the other side.

It is suggested that in certain cases no matter what the treatment the result may be bad.

One of the patients, B. S., reported in the group of patients receiving miscellaneous treatment, had on admission to the hospital involvement of both sides, with a history of symptoms on one side for fourteen months and on the other for seven months. She had severe muscular spasm and protected both hips with greatly limited motion, and the one involved for the longest period was practically fixed. Roentgenograms showed what was interpreted as 1.5 cm. displacement on the two sides with pronounced narrowing of the joint on the one side and moderate narrowing on the other.

Despite traction for five months, the worse side remained practically immobile, and subsequent exploration at the time of arthroplasty showed almost complete degeneration of the joint. At no time was the head dense, which indicated aseptic necrosis.

Did this degenerative process arise solely from traumatic arthritis? It seems that in certain instances there is some factor other than interference with circulation to the head of the femur and traumatic arthritis which influences the result in slipped epiphysis.

I have had no experience with drilling or with subtrochanteric osteotomy for slipped epiphysis. If drilling is done I believe it should be accompanied by skeletal fixation. Subtrochanteric osteotomy is an unanatomic makeshift procedure, but it may have its place in certain cases in which the head has healed in a deformed position.

SUMMARY

In a consecutive series of 26 patients with slipped upper femoral epiphysis in 36 hips, the results in 28 of the hips have been assessed after an average of six and three-tenths years.

In 10 patients the condition was bilateral.

Early diagnosis before significant displacement occurs is the key to the problem.

In adolescence limp with pain in the hip, thigh or knee, which is often intermittent at the start, is suggestive, particularly if the child is obese.

Reduced internal rotation, abduction and flexion of the hip with pain and spasm in the extremes of these motions are early physical findings.

Early roentgen findings are rarefaction in the metaphysial region and anterior displacement of the neck on the head, as seen in the lateral view.

Various methods of treatment, which are assessed in this report, include the following: (*a*) In those hips with minimal to moderate displacement the best results were obtained by a method using a particular combination of traction and plaster fixation. (*b*) In hips with minimal displacement nailing in situ without arthrotomy gave good results. (*c*) In those hips with severe displacement, open reduction with skeletal fixation gave good results provided certain technical criteria, which are described, were met. (*d*) Closed manipulative reduction did not seem to be a good method.

All satisfactory methods of treatment consider the mechanism of displacement and maintain the circulation to the head of the femur.

If the patient is obese, reduction of weight is helpful in the treatment.

The final evaluation of the results in slipped epiphysis depends on the adult experience of the patients.

ABSTRACT OF DISCUSSION

DR. FREMONT A. CHANDLER, Chicago: Dr. Green's presentation of slipped femoral epiphysis brings into sharp focus a clinical entity that has become blurred by the rapid swing of therapy from conservative treatment to radical operation and back again. The approach to cases of slipped femoral epiphysis should be individual and the procedures adapted to the need of each case. The duration and degree of the deformity as well as the condition of the epiphysial plate will determine the outcome.

If reduction and fixation can be accomplished by gentle means, such should prevail. Capsular and vascular changes will be minimal and function of the joint preserved. However, if the deformity is older and more fixed, manipulation will only add insult to the already changed joint.

Correction by osteotomy of the neck of the subtrochanteric area is in order. Surgical damage to the circulation of the epiphysis must be avoided. This means that the soft structures along the posterior aspect of the femoral neck should not be overstretched or divided. Cuneiform osteotomy distal to the epiphysial line accomplishes reduction with the least trauma.

Fixation by position with the hip in a plaster splint or, better still, some form of internal fixation is necessary.

I find nothing to disagree with and I approve wholeheartedly of Dr. Green's presentation.

I should like to inquire as to the duration of traction following open reduction in Dr. Green's older cases. When is weight-bearing activity permitted in the group of older cases? From his description I gathered it was about ten months. I should like to have him emphasize that. What are the exercises which he advocates for this particular group of cases? He might clarify them a bit by describing them briefly.

This is a timely paper. The condition is being encountered right along, and the results have not been as satisfactory as they should have been.

DR. WALTER P. BLOUNT, Milwaukee: This is a controversial subject because the results are so variable. In some cases, with little or no treatment the results are brilliant. In others, with the most energetic treatment the results are catastrophic. For this reason the study of any small series of cases is almost valueless. This is one of the best collections of cases that I have seen, and its analysis is praiseworthy.

The treatment as outlined in the first part of the discussion is probably the best for the physician who is not expert in surgical operations on the hip or who has not the facilities for the more radical procedures. I admit that it is not ideal, from either a medical or a surgical standpoint and certainly not from an economic one. Among the early cases in which treatment was conservative I saw some disasters. The last slipped femoral epiphysis which I treated by traction and a cast became stiff in severe deformity. I think that this ankylosis was inevitable. I am glad that I did not operate.

My friends who were using the flanged nail for internal fixation of incompletely slipped heads which did not need reduction or incompletely slipped heads following open reduction had such bad results that I was influenced in subsequent cases to use another type of fixation, with the smaller Moore nails. These are more adaptable in the treatment of various conditions of the hip. In slipped femoral epiphysis, multiple small nails or screws are superior to the single large nail. The reason is that in this condition the metaphysial surface, which seems so soft in the roentgenogram, is actually so hard that it is difficult to drive any nail through it. The most satisfactory procedure is to drill pointed nails or screws across the line. This entails a minimum of trauma.

DR. J. WARREN WHITE, Greenville, S. C.: I want particularly to emphasize the value of traction. In 1 case which I observed what looked like a congenital coxa vara was really a gradually developed coxa vara, or a slow slipping of the epiphysis.

This case is representative of a series of 3 in which the behavior of the hip was exactly alike. By main strength the epiphysis was wrenched off, and after traction with about 25 to 30 pounds (11 to 14 Kg.) had been used for a month, the head could be pulled up into a fairly satisfactory position.

And I can prove that all the blood supply to the head was not ruined. Constant traction over several weeks pulled out the capsular cuff so that there was tissue through which enough vessels passed to keep the head in good condition.

Four and a half years afterward the child whose case is presented here was still perfectly normal. The fifty year end result will be interesting, but I have described this case simply to emphasize what I feel is an extremely important point, that is, maintenance of real traction over a long period, at least during the acute convalescence.

DR. WILLIAM T. GREEN, Boston: Dr. Chandler asked about the use of traction after open reduction. Since I am concerned about the circulation of the head of the femur, I have made every effort to follow my patients after open reduction and have them kept in traction about six weeks after operation, starting motion while they were still in traction. In general I have allowed weight bearing with crutches at the end of three months—that is, partial weight bearing—with motions and use of the leg in about three months and full weight bearing in six months.

If there is evidence of aseptic necrosis, as in my early cases, of course the follow-up period is long indeed, and such changes should be recognized at their inception—that is, before the head is crushed—if aseptic necrosis exists.

Patients treated by the traction-spica-traction method are allowed to walk with crutches on an average of five months after the treatment is started. The average interval for weight bearing without crutches averaged seven and one-half months, with full activity in an average of eleven and one-half months. All intervals date from the start of treatment.

Dr. Chandler asked the purpose of the exercises after the removal of the spica for those patients treated by the traction-spica-traction method. They are designed to increase motion in the hip joint, to develop strength in the gluteus maximus and the abductor muscles of the hip and secondarily to promote calcification in the involved area. The exercises are active, not passive. Traction which is counterpoised allows active motion and is an excellent way to start early activity. Underwater exercises may be used if convenient.

Dr. Blount mentioned 1 patient who did badly. On occasion it would seem that an unknown factor enters into the prognosis. Incidentally, a hip which does not loosen up with traction should not be placed in a spica.

Dr. Blount mentioned the economic consideration involved in the longer period of hospitalization demanded by the traction-spica-traction method. The period of hospitalization is much reduced by the fact that in practice the period in which the patient is in the spica is ordinarily spent at home. This treatment takes longer, but if the results are better the increased time is justified.

As regards the use of skeletal fixation for those hips with minimal displacement, I think it would be well if the patients have spasm first to institute traction including internal rotation until the muscular spasm is alleviated or minimal. It is true that skeletal fixation by methods other than the flanged nail may be less traumatic. I believe too that partial weight bearing with crutches for a considerable period after the fixation is desirable and may improve the result in these hips. The results in the hips with minimal displacement which were treated by skeletal fixation have been good; but at this time they do not seem quite as good as those treated by the traction-spica-traction method. The final evaluation, however, must depend on the comparative lifetime performance of the hips.

Dr. White's case is most interesting. I believe that if one proposes to change the position of the head the use of traction with internal rotation is much less likely to produce aseptic necrosis than is manipulation with the patient under anesthesia. It is well to recall that the result in any case may be good in spite of the treatment.

EVALUATION OF GELATIN AND PECTIN SOLUTIONS AS SUBSTITUTES FOR PLASMA IN THE TREATMENT OF SHOCK

HISTOLOGIC CHANGES PRODUCED IN HUMAN BEINGS

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A substitute for plasma in the treatment of shock ideally should increase the reduced blood volume without producing significant untoward effects. Only the presence of large molecules which retain the injected fluid within the circulation produces a sustained rise of the blood volume. Such hydrophilic colloidal solutions have been observed to produce undesirable side effects; therefore, these side effects should be evaluated before the solutions are used as plasma substitutes.

Increase of the blood volume with solutions devoid of red cells reduces the red cell concentration, as measured by the hemoglobin concentration or the hematocrit value. Hemodilution is easily recognized by simple laboratory methods, which are sufficiently accurate for clinical evaluation to substitute for the elaborate methods for determination of the blood volume. The production of hemodilution then can be used as a criterion for the efficiency of a plasma substitute in the treatment of shock.

Among the undesirable effects of macromolecular substances pseudoagglutination of erythrocytes, as recognized by rouleau formation [1] and rise in the sedimentation rate, has been observed and reported.[2] Recently, Hueper [3] described a "hematologic" reaction due to intravenous administration of macromolecular substances; it is characterized by anemia, leukopenia or leukocytosis, impairment of coagulation, thrombopenia, hemorrhagic diathesis and increase in agglutination and sedimentation rate of erythrocytes. A second important reaction is that of the tissues, chiefly as the result of deposition of macromolecular substances in the organs. Acacia (used as a plasma substitute in the first World War and more recently in the treatment of nephrosis) was found deposited in the liver; [4] Hueper [5] saw characteristic changes after the administration of other macromolecular substances as well.

To these criteria should be added the therapeutic results on patients in shock, the occurrence of pyrogenic and other clinical reactions, the problem of antigenicity, the effect on the function of the liver and kidneys and the results of experiments on animals, especially of those

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dealing with shock due to hemorrhage, trauma and burn.

In the past years extensive work along these lines has been performed on isinglass,[6] gelatin[7] and Pectin.[8] In the Hektoen Institute investigations with the administration of pectin and gelatin solutions to patients in shock and to hospital control subjects were conducted, and the impression was gained that the two solutions are equally effective in the treatment of shock.[9] For a reliable comparison between the solutions —which is the object of this presentation—data on hemodilution, pseudoagglutination of erythrocytes (as an example of the hematologic alterations) and tissue changes were selected from a variety of studies, which have been partly reported elsewhere.[10]

MATERIAL AND METHODS

The studies are based on experience with the intravenous administration of 257 liters of gelatin solution to 162 patients in 213 individual infusions; the quantity of solution administered ranged from a total of 1 to 10 liters per patient. Pectin solution was administered in the amount of 235 liters to 155 patients in 251 individual infusions, for a total of from 1 to 9 liters per patient. About half of the patients were hospital control subjects; the other half were patients with various degrees of surgical, traumatic, hemorrhagic and medical shock. The clinical details have been discussed elsewhere.[11] For these patients the concentration of hemoglobin (determined by a photoelectric colorimeter), the hematocrit value and the sedimentation rate of the red cells (both measured by the Wintrobe tube) were determined before, immediately after and twenty-four hours after the infusions. The mean corpuscular hemoglobin concentration was calculated according to the equation of Wintrobe.[12] The percentage change in the hemoglobin concentration, hematocrit value and mean corpuscular hemoglobin concentration, determined before

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9. Kozoll and others.[7o] Meyer and others.[8f]

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11. Kozoll and others.[7o] Meyer and others.[8f]

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and after administration of the hydrophilic colloid, was used for purposes of comparison. The other clinical and laboratory data obtained on these patients are not considered in this study.

From 4 patients who had received gelatin solution and from 3 who had received pectin solution, biopsy specimens of the liver were obtained at various intervals after the infusion on the occasion of a laparotomy, which was indicated by the underlying disease. Autopsy material was obtained from 12 patients who had received various doses of gelatin solution and from 10 who had

TABLE 1.—*Average Percentage Change of Hematocrit Value, Hemoglobin Concentration and Mean Corpuscular Hemoglobin Concentration*

	Gelatin		Pectin	
	Hospital Controls	Patients in Shock	Hospital Controls	Patients in Shock
Number of cases	75	77	61	73
Average percentage decrease of hematocrit value after administration of:				
1,000 cc.	11.6	19.5	10.3	18.8
2,000 cc.	17.1	....	15.9	....
3,000 cc.	19.3	....	16.1	....
Average percentage decrease of hemoglobin concentration after administration of:				
1,000 cc.	8.5	16.4	6.7	14.7
2,000 cc.	12.6	....	12.8	....
3,000 cc.	18.8	....	14.8	....
Average percentage increase of mean corpuscular hemoglobin concentration after administration of:				
1,000 cc.	0.31	0.88	1.0	1.8
2,000 cc.	2.0	....	1.2	....
3,000 cc.	0.1	....	2.8	....

received pectin solution at different intervals before their death.

The gelatin (with an average molecular weight of approximately 35,000) was provided by the Upjohn Company (Kalamazoo, Mich.) in 5 per cent solutions; one solution consisted of 5 per cent gelatin in isotonic solution of sodium chloride, another of 5 per cent gelatin in 5 per cent dextrose solution and another of 5 per cent gelatin fortified with tryptophan, tyrosine, methionine and cystine. The gelatin was prepared from bone collagen by a process of electrodialysis. The calcium gelatinate was then autoclaved, mixed with distilled water, sodium hydroxide, phenylmercuric borate and sodium chloride, passed through a sterilizing filter and autoclaved again. The p_H of the end product was of physiologic range, with a viscosity of 2 centipoises and an oncotic pressure of 70 mm. of mercury (± 5 mm.). The pectin solutions were prepared by Frederick Stearns & Company (Detroit) in 0.9 per cent sodium chloride; the molecular weight was around 55,000. The viscosity varied between 3.55 and 4.68 centipoises; the p_H ranged between 3.91 and 3.70. The original pectin, which is obtained from citrus fruit, is a carbohydrate-like substance composed of a long-chained molecule consisting chiefly of polymerized galacturonic acid molecules with the addition of various smaller groups. Its molecular weight varies between 45,000 and 60,000 and is reduced from 250,000 by autoclaving in the process of preparing the solution. Hueper [5a] emphasized the difference in the reactions elicited in the tissues by pectin solutions of different molecular weights. The pectin solutions were adjusted by phosphate buffers to a p_H of about 7.2 before intravenous administration.

OBSERVATIONS ON HUMAN BEINGS

I. Hemodilution.—Gelatin and pectin solutions were equally efficient in producing hemodilution, as indicated by the percentage change of hemoglobin concentration or hematocrit value after the administration of comparable amounts (table 1). Both substances produced more severe hemodilution in patients in shock than in hospital control subjects. There was a difference in the degree of hemodilution as determined by the hemoglobin concentration or the hematocrit value; the hematocrit level dropped more in all instances than the hemoglobin concentration did. Consequently, the mean corpuscular hemoglobin concentration increased equally with each solution after its administration both to patients in shock and to those not in shock. The increase appears for mathematical reasons less marked if the mean of the individual concentrations is taken than if it is calculated from the average of the hematocrit values and hemoglobin concentrations.

Administration of additional gelatin or pectin solution over the initial 1,000 cc. produced much less hemodilution in all the instances recorded.

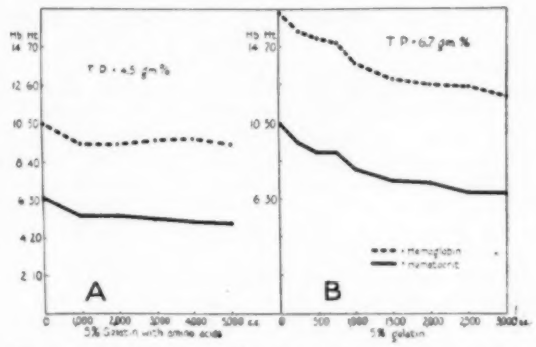

Fig. 1.—Serial determinations of the hematocrit and hemoglobin values following continuous infusions of gelatin solution to a hypoproteinemic patient (*A*) and a person with acute alcoholism (*B*). The inability to produce significant hemodilution in patient *A*, whose protein and hemoglobin reserves were depleted, is apparent. Patient *B*, whose protein and hemoglobin values were normal, shows progressive hemodilution, which tends to decrease with increasing amounts of fluid. The total protein content for patient *A* is 4.5 Gm. and for patient *B* 6.7 Gm. per hundred cubic centimeters.

Consistently with both substances the hemodilution curve leveled off. The leveling off was not uniform, in contrast to the initial percentage change of hemoglobin concentration and hematocrit value, which was similar in all cases observed. In an attempt to establish the tendencies responsible for these variations of the hemodilution curve after administration of larger amounts, we found that for patients with anemia or hypoproteinemia the hemodilution curve leveled off

much earlier than for patients with a normal blood count and adequate protein reserves (fig. 1).

II. Sedimentation Rate of Erythrocytes.—The sedimentation rates of almost all patients rose after the administration of gelatin or pectin solution (table 2). The rise was of about equal degree for the two groups. The sedimentation rates of patients in shock increased more than those of hospital control subjects, because the initial sedimentation rates of the patients in shock were lower, which permitted a higher rise. Again,

TABLE 2.—*Influence of Intravenous Administration of Gelatin and Pectin Solutions on the Sedimentation Rate of Erythrocytes*

	Gelatin		Pectin	
	Hospital Controls	Patients in Shock	Hospital Controls	Patients in Shock
Number of cases	75	77	61	73
Average increase of the sedimentation rate in mm. per hr. after administration of:				
1,000 cc.	15.1	23.8	12.6	24.3
2,000 cc.	17.9	....	20.0	....
3,000 cc.	20.3	....	18.6	....

TABLE 3.—*Results of Histologic Examination of Organs of Patients Who Had Received Various Amounts of Gelatin*

Age	Race	Sex	Clinical Diagnosis	Amount Injected, Cc.	Number of Injections	Interval Between First Injection and Examination	Liver	Spleen	Kidney
45	W	M	Carcinoma of the bladder	6,000	2	3 days	—	—	vvv*
70	W	M	Ieteric cirrhosis; ascites	4,200	2	60 hours	—	—	vv
55	W	M	Carcinoma of prostate	3,000	1	12 hours	—	—	vv
33	W	F	Carcinoma of cervix uteri	2,300	2	4 hours	—	—	—
21	W	F	Thrombosis of splenic vein; hypoproteinemia	9,000	7	26 days	—	—	—
60	W	M	Carcinoma of stomach	3,000	3	66 days	—	—	—
44	W	F	Carcinoma of cervix uteri	4,000	3	18 days	—	—	—
63	W	M	Carcinoma of stomach	5,000	3	9 days	—	—	d†
50	W	M	Bacterial endocarditis	3,000	2	4 days	—	—	—
45	W	M	Toxic hepatitis	1,200	1	12 hours	—	—	—
68	W	F	Coronary occlusion	1,000	1	12 hours	—	—	—
37	W	F	Carcinoma of cervix uteri	1,200	1	10 hours	—	—	—
45	W	M	Carcinoma of stomach	1,000	1	8 hours	—	Biopsy	
48	W	F	Obstructive jaundice	1,000	1	6 hours	—	Biopsy	
51	W	F	Pyloric obstruction	2,000	2	2 days	—	Biopsy	
36	W	M	Bleeding peptic ulcer	2,000	2	6 days	—	Biopsy	

* v indicates vacuolation of the tubular epithelial cells.
† d indicates dilatation of the glomerular spaces and tubules.

TABLE 4.—*Results of Histologic Examination of Organs of Patients Who Had Received Various Amounts of Pectin*

Age	Race	Sex	Clinical Diagnosis	Amount Injected, Cc.	Number of Injections	Interval Between First and Last Injection	Interval Between Last Injection and Examination	Liver	Spleen	Kidney
30	N	F	Intestinal obstruction	2,000	1	.....	8 hours	—	—	ddd ‖
65	N	F	Carcinoma of colon	2,000	2	1 day	12 hours	—	—	d
43	W	M	Nephrosis; hypoproteinemia	9,000	9	19 days	3 days	vvv* p†	pppp e‡	pppp
15	N	M	Nephrosis; hypoproteinemia	7,000	14	15 days	26 days	vv pp	pppp eeee	pppp
72	W	M	Decubital ulcers; sepsis	4,300	5	14 days	18 days	—	ggg § eeee ppp	—
73	W	M	Injury to spinal cord; paraplegia	6,000	3	8 days	20 days	—	gg e	p
49	W	M	Carcinoma of stomach	6,000	3	3 days	2 days	—	—	—
55	W	M	Intestinal obstruction	4,000	2	1 day	12 days	—	—	—
48	W	F	Peritonitis	2,000	2	.....	2 days	—	—	—
79	N	M	Carcinoma of stomach	2,000	2	1 day	1 day	—	—	—
21	N	M	Sickle cell anemia; hepatitis	1,000	1	.....	1 day	—	Biopsy	
55	W	F	Carcinoma of stomach	2,000	2	.....	1 day	—	Biopsy	
40	W	M	Bleeding peptic ulcer	1,000	1	.....	1 day	—	Biopsy	

* v indicates vacuolation.
† p indicates deposition of a material staining with ruthenium red.
‡ e indicates endothelial cell proliferation.
§ g indicates giant cells.
‖ d indicates diuresis.

rise of the sedimentation rate did not continue with additional administration of gelatin and pectin solutions, and the third liter of both substances had almost no effect.

III. Changes in the Tissues in Human Beings.—A. Gelatin: A morphologic change possibly attributable to the administration of gelatin which was observed in the organs examined (liver, kidney, spleen, heart, lung and adrenal gland) was vacuolation of the epithelium of the proximal and distal convoluted tubules of the kidney (table 3). The vacuoles were uniform and about half the size of a red cell. They crowded the epithelial cells, the nucleus being displaced to the base of the cells. The vacuoles failed to give a reaction for fat. They were not stained by Mallory's aniline blue stain or by ruthenium red. This change was observed in 3 patients who had received 6,000, 4,200 and 3,000 cc. of solution within the last one to three

days before their death. In the patient who had received 3,000 cc. in one infusion one day before death, a homogeneous material, which stained blue with hematoxylin and eosin, was seen in the greatly widened glomerular spaces and also in the dilated tubules of the kidney (fig. 2). In other patients, to whom smaller amounts were administered or for whom the interval between death and the last injection of gelatin solution was longer, this change was not observed. It should be stressed that a patient who had received 2,300 cc. within the last thirty-six hours did not reveal this change, nor did another patient who had received 3,000 cc. three days before death.

Fig. 2.—Kidney of a patient who had received 3,000 cc. of gelatin solution twelve hours before death. The glomerular space and the tubular lumen are greatly dilated. The glomerular space is filled by blue-stained material. The epithelium of the convoluted tubules is extensively vacuolated.

B. Pectin: In the examined organs (heart, lung, spleen, liver, pancreas and kidney) of the patients who had received injections of pectin solution the following changes were encountered which could be attributed to the administration of pectin (table 4):

1. Dilatation of glomerular spaces and tubular lumens. The glomerular loops appeared to be immersed in the content of the widened glomerular spaces and compressed by it. The lumens of the tubules belonging to these glomeruli were also greatly widened. This picture, which simulates that seen in experimental animals during forced diuresis, was especially noticeable in 2 patients who had received 2,000 cc. of pectin solution eight and twelve hours before death. In patients with a longer interval between the last injection of pectin solution and death these changes were not present.

2. Deposition of a peculiar material in organs with a cellular reaction. These depositions were observed in 4 patients who had received 4,300, 6,000, 7,000 and 9,000 cc. of the pectin solution with an interval of thirty-two, twenty-eight, forty-one and forty-nine days, respectively, between the first administration and death. In 1 patient, however, who had received 6,000 cc. with an interval of only five days between the first infusion of pectin solution and death, they were not observed. Altogether, in patients who had received less than 4,000 cc. of pectin solution or for whom not more than thirteen days had elapsed between the first infusion and death, no changes were encountered which possibly could be attributed to administration of pectin.

A characteristically stained structureless material was found in the pulp of the spleen (producing a variable degree of splenomegaly), in Kupffer cells and portal triads of the liver, in glomerular loops and in lumen of tubules of the kidney and in capillaries and proliferated mononuclear cells of the lung. Histologically, the picture resembled amyloidosis. The material appeared purple in sections stained with hematoxylin and eosin, pink (different from the distinct red of the collagenous fibers) with Van Gieson stain and blue with Mallory's aniline blue stain. It did not give a reaction for amyloid, iron or calcium and it was not acid fast. In sections stained with ruthenium red,[13] described as a specific stain for pectin,[14] the material appeared selectively distinctly red. It was not digested if the method of Bjorkenheim[15] was used. Smears of the pectin solution on glass slides were stained by ruthenium red but not by hematoxylin and eosin, Van Gieson stain or Mallory's aniline blue stain.

The deposition was accompanied by proliferation of reticulum cells and endothelial cells in the spleen, by proliferation of glomerular cells in the kidney with formation of giant cells and hyalinization of the loops and by mobilization of the Kupffer cells in the liver.

The changes varied greatly in the 4 patients, whose cases therefore are summarized:

REPORT OF CASES

CASE 1.—A 15 year old Negro youth gave a history of extensive pitting edema for over a week and occasional dizziness and dyspnea on slight exertion. The essential findings on admission to the hospital were edema, anemia, a blood pressure of 114 systolic and 84 diastolic and albuminuria; examination of the serum revealed a nonprotein nitrogen content of 54 mg. per hundred cubic centimeters and a total protein content of 3.7 Gm. per hundred cubic centimeters with an albumin-globulin ratio of 0.97; the value for cholesterol was 386 mg. per hundred cubic centimeters. He was given plasma and later pectin solution (7,000 cc. in fourteen infusions, the last twenty-six days before death) in an unsuccessful attempt to reduce the edema. Nine weeks after his admission to the hospital the blood pressure rose to 150 systolic and 105 diastolic. The spleen became greatly enlarged, and the patient died with symptoms of uremia. (A few days before death the serum nonprotein nitrogen content was 65 mg. per hundred cubic centimeters, with a total protein content of 2.7 Gm.). The pathologic diagnosis included acute glomerulonephritis with superimposed subacute glomerulonephritis, splenomegaly (1,005 Gm.) with a large infarct of the lower pole of the spleen, extreme generalized anasarca and pronounced dilatation of the left ventricle.

Histologic examination revealed in the pulp of the spleen large, irregularly outlined deposits of a material which stained purple with hematoxylin and eosin and red with ruthenium red. The deposition was diffuse, with only a few islands of pulp left intact. The staining of the material varied in intensity. In some places it appeared homogeneous and in others broken into smaller lumps; it even formed meshes in which isolated reticulum cells were embedded. The latter were irregularly proliferated and formed even multinuclear giant cells with much cytoplasm. Connected with the edge of the large deposits were irregularly interwoven fine strands of strongly colored material, which were arranged around apparently imbibed reticulum fibers. The sinuses appeared greatly dilated and usually contained mobilized cells only. In places, however, the material was found within the dilated sinus, surrounded by proliferated endothelial cells, which may form multinuclear giant cells and be mobilized from the wall. The giant cells were arranged in aggregates and contained in their cytoplasm or engulfed the material stained with ruthenium red. The lymph follicles were scarce and small (fig. 3*A*).

The glomeruli of the kidney were much smaller than normal. Their tufts were irregularly arranged and often matted together and adherent to the glomerular capsule. In places, proliferation of the glomerular cells and sclerosis of the loops were seen. Many loops were obstructed by thick, darkly stained plugs which gave a ruthenium red reaction. In those areas the entire wall of the loop was thickened and gave a lighter ruthenium red reaction. The glomerular cells were scarce. Some of these infiltrated loops were adherent to each other and to the capsule. These foci were surrounded by proliferated glomerular cells and sclerotic connective tissue fibers, appeared dark blue with hematoxylin and eosin and gave a pronounced ruthenium red reaction but revealed also calcification with Von Kossa's stain. Some material stained with ruthenium red was found in the glomerular space; also in the often dilated tubules concentrated casts with a distinct ruthenium red reaction were encountered. Extensive proliferation of the intertubular connective tissue, occasionally with cellular infiltration, was noted throughout and was due to subacute nephritis (fig. 3*B*).

The hepatic cell cords showed a normal appearance. Some of the Kupffer cells were irregularly shaped, sometimes appearing as giant cells, and were mobilized from the hepatic cell cords. Their cytoplasm contained one or more droplets which stained with ruthenium red. Occasionally in enlarged portal triads capillaries were obstructed by plugs of ruthenium red–staining material; the same material was deposited in proliferated connective tissue fibers.

Also, in the lung some dilated capillaries in the alveolar septums contained plugs that stained with ruthenium red. Around them multinucleated giant cells were found which contained ruthenium red–staining material.

13. The following procedure was used: Deparaffined sections were stained for one minute with a freshly prepared 1 per cent aqueous solution of ruthenium red (Coleman & Bell Company, Norwood, Ohio), washed with distilled water, brought through alcohol and xylene and mounted in Canada balsam.

14. Mangin, M. L.: Sur les reactifs colorants des substances fondamentales de la membrane, Compt. rend. Acad. d. sc. **111**:120, 1890; Sur l'emploi du rouge de ruthenium en anatomie vegetale, ibid. **116**:653, 1893. Tobler, F.: Ueber die Brauchbarkeit von Mangins Rutheniumrot als Reagens für Pektinstoffe, Ztschr. f. wissensch. Mikr. **23**:182, 1906. Hueper.[5a]

15. Oldenburg, R., quoted by Romeis, B.: Taschenbuch der mikroskopischen Technik, Berlin, R. Oldenbourg, 1932.

Case 2.—A 43 year old white man had been treated for glomerulonephritis for the past two years. He was admitted to the hospital with puffing edema of the face and extremities. The blood pressure was 130 systolic and 90 diastolic. His urine contained much albumin and some red cells and lipoid casts. The serum showed a nonprotein nitrogen content of 62 mg. and a creatinine content to 5.6 mg. per hundred cubic centimeters; the total protein content fell to 2.6 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 0.9. The patient died with uremic symptoms. At autopsy chronic glomerulonephritis with nephrotic component, general anasarca and passive congestion were found. The spleen weighed 235 Gm.

Fig. 3.—*A*, spleen in case 1. Large, irregularly outlined deposits of ruthenium red–stained material are seen in the pulp of the spleen. The sinuses are dilated and contain in places the same material surrounded by large multinuclear giant cells. *B*, kidney in case 1. The loops of the glomeruli are obstructed by darkly stained plugs which give a strong reaction with ruthenium red. The wall of the loops has imbibed similar material, and appreciable sclerosis and calcification are present.

content of 5.2 mg. per hundred cubic centimeters; the total protein content was 3.8 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 0.9. In a frustrated attempt to correct the edema, he was given within forty-six days 9,000 cc. of pectin solution in nine individual infusions, the last one three days before death. The nonprotein nitrogen content (determined a few days before death) rose to 87 mg. and the creatinine

Histologically, in the pulp of the spleen the characteristic material was diffusely deposited in the form of a dense interlacing network with threads of variable thickness. Some of them were wide, homogeneous and less deeply colored, and others were thin and deeply colored; they were apparently due to infiltration of reticulum fibers. No reaction of the cells of the pulp was noted. The scarce sinuses were free of the material

and revealed extensive proliferation of the endothelial cells. The lymph follicles contained only a small center of lymphoid elements, which was traversed by fibers giving a reaction with ruthenium red. This center was surrounded by a hemorrhagic zone, which was followed by an area with diffuse deposition of material stained with ruthenium red, in which, however, the shadows of the follicular structure were still apparent. The larger vessels and trabeculae were almost entirely surrounded by the characteristic material.

The glomeruli of the kidney were usually enlarged. In the lumens of the loops in places plugs densely stained with ruthenium red were seen. The walls of the loops appeared as a whole greatly thickened and homogeneous but gave a less strong reaction to ruthenium red and also to Mallory's aniline blue than the plugs. Only a few nuclei were usually seen around the swollen walls of those loops in which a basement membrane could not be made out. The loops were often matted together and surrounded by cellular reaction (fig. 4 *A*). In places multinuclear giant cells, apparently derived from glomerular cells, were seen on the surface of the swollen loops. Ruthenium red–stained material was scarce in the capsular space. Some glomeruli underwent sclerosis, and here some fibers appeared soaked with the characteristic material. In the tubules concentrated casts with a strong ruthenium red reaction were noted. The intertubular connective tissue was increased and revealed lymphatic infiltration.

The liver showed small central areas of necrosis. In the intact areas the hepatic cell cords revealed many vacuoles which did not give a ruthenium red reaction.

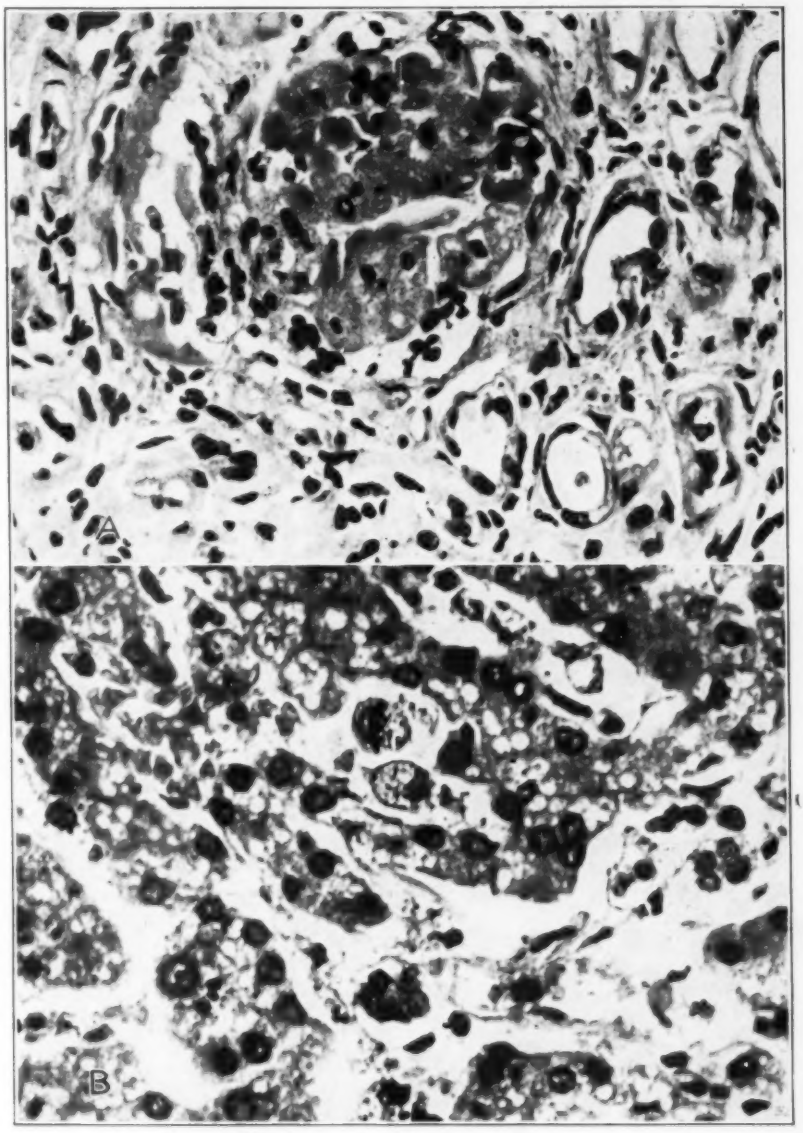

Fig. 4.—*A*, kidney in case 2 (high power). There are noticeable widening of glomerular loops, due to uniform imbibition with ruthenium red–stained material, and cellular reaction around the loops. *B*, liver in case 2 (high power). There is vacuolation of the cytoplasm of mobilized large Kupffer cells lying in the sinuses. The vacuoles give a reaction with ruthenium red.

The Kupffer cells, however, were often considerably enlarged and bizarre in shape. Their abundant cytoplasm contained several droplets which were stained by ruthenium red (fig. 4 *B*). Occasionally imbibition of connective tissue fibers with the characteristic material was noted in the portal triads.

Case 3.—A 72 year old white man was admitted to the hospital with senile arteriosclerosis, dementia, debility, a large decubital ulcer over the sacrum and extensive furunculosis. As an adjunct to fluid therapy, the patient received 4,300 cc. of pectin solution in five injections. He succumbed with symptoms of bronchopneumonia.

At autopsy bronchopneumonia of the lower lobe of the left lung, hemorrhagic cystitis and moderate dilatation of both ventricles of the heart with passive congestion were found. The spleen weighed 230 Gm.

Histologically, the picture of the spleen was dominated by proliferation of endothelial and even more of reticulum cells with formation of large multinuclear cells of the character of foreign body giant cells. The pulp cords were often almost replaced by the proliferated reticulum cells. Many sinuses were free, whereas others were dilated and filled entirely by the large, irregular endothelial cells (fig. 5 *A*). Between the proliferated reticulum cells and occasionally between the endothelial cells small amounts of material stained with ruthenium red were seen, mostly in shredded form. The cells engulfed and sometimes included it (fig. 5 *B*). Only small areas of intact pulp were seen. The lymph follicles were small and compressed.

The glomeruli of the kidney were only slightly enlarged, and some showed in places proliferation of cells; others were sclerotic. In some of the loops were plugs

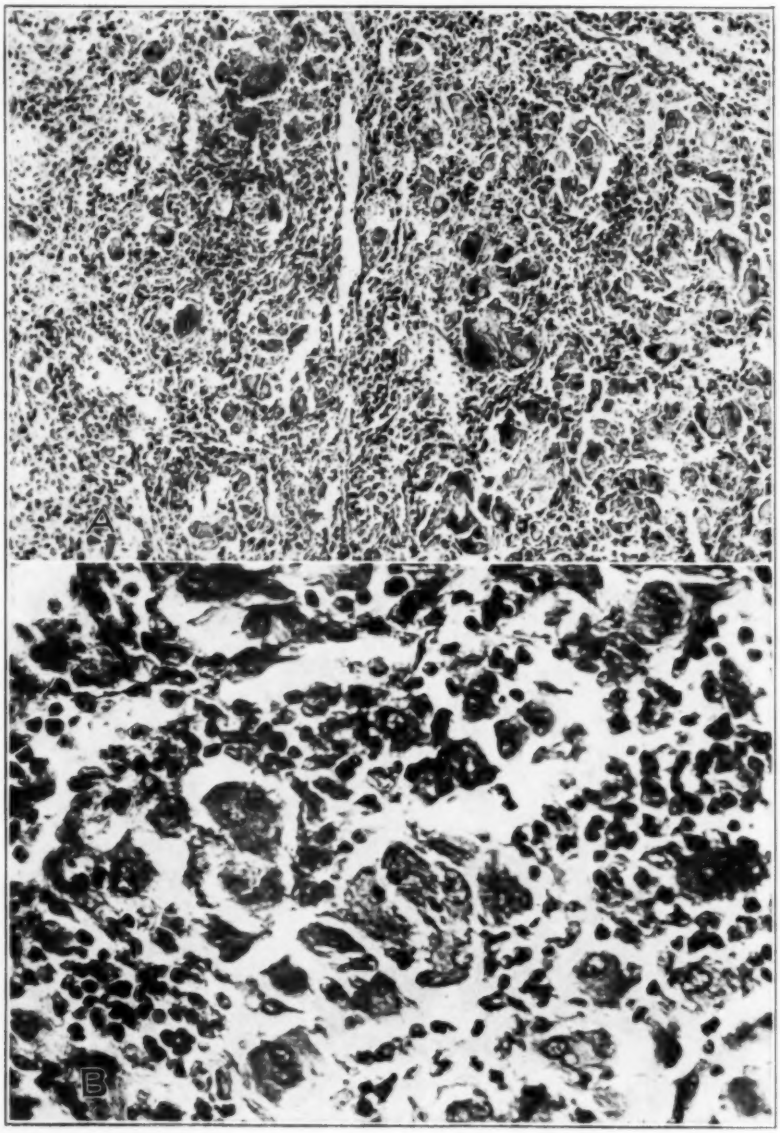

Fig. 5.—*A*, spleen in case 3 (low power). Extensive proliferation of the reticulum and endothelial cells with formation of giant cells obscures the normal architecture. *B*, spleen in case 3 (high power). Proliferation of reticulum cells with formation of giant cells surrounds shredded ruthenium red–stained material. A sinus is free.

densely stained with ruthenium red, around which formation of giant cells was noted. Similar material was found in Bowman's spaces and in the form of casts in tubules. The interstitial tissue revealed focal infiltration with lymphocytes and plasma cells.

In the liver, which revealed small foci of necrosis and fibrosis of the portal triads, some Kupffer cells contained droplets stained with ruthenium red.

CASE 4.—A 73 year old white man gave a history of fracture of the spine fifty years ago with subsequent flaccid paralysis of both lower extremities. He was admitted with large decubital ulcers over the sacrum and died with signs of septicemia. Among other fluids 6,000 cc. of pectin solution was given in three infusions.

The essential changes noted at autopsy were: dilatation of the left ventricle of the heart with brown atrophy, chronic passive congestion, arteriosclerosis of the aorta and coronary arteries and old compression fracture of the eleventh and twelfth dorsal and first lumbar vertebra. The spleen weighed 225 Gm.

Histologically the structure of the pulp and the follicles in the spleen was in general preserved. Only in small scattered foci a proliferation of reticulum and also of endothelial cells was noted, with formation of foreign body giant cells. Small amounts of irregularly formed ruthenium red–stained material were surrounded by the proliferated cells, which were seen in the pulp and only rarely filled a dilated sinus (fig. 6).

In tubules of the kidney ruthenium red–stained casts were seen; otherwise, no changes attributable to the administration of pectin were encountered in the kidney or the liver.

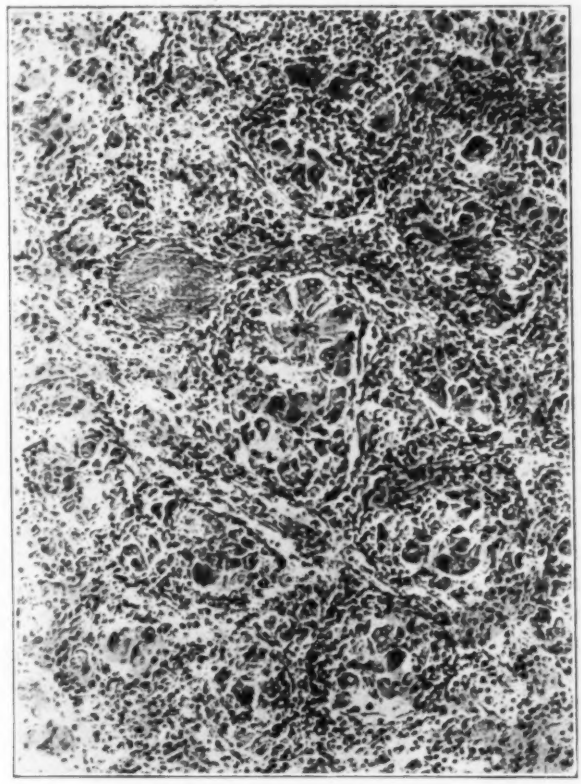

Fig. 6.—Spleen in case 4. Foci of proliferated reticulum cells with formation of giant cells engulf some ruthenium red–stained material.

CHANGES IN THE TISSUES IN EXPERIMENTAL ANIMALS

Five rabbits which had received 230 to 480 cc. of gelatin solution over a period from twelve to thirty-eight days and which were killed shortly afterward showed no changes in the tissues attributable to administration of gelatin except for some proliferation of Kupffer cells in the liver and alveolar cells in the lung in the rabbit which had received the largest amount.

Of 5 rabbits which had received 295 to 865 cc. of pectin solution within twelve to eighty-six days, 1 showed marked splenomegaly. All of them revealed alterations of various intensity which were similar to those observed in cases 1 and 2. The changes found in the spleen and kidneys and the amount of material stained with ruthenium red far exceeded those found in human beings.

COMMENT

The gelatin and pectin solutions used produced a comparable hemodilution (which probably means increase in blood volume) as far as degree, duration and relative leveling off of the hemodilution curve with use of larger doses are concerned. The results of quantitative com-

parison agree with the impression gained from clinical observations of patients in shock. This deserves emphasis because the gelatin and the pectin solution used differed greatly in chemical nature, in concentration and even in physical characteristics. The condition of the patient, namely the presence of shock, influences the results more than the nature of the macromolecular solution. Of the first 1,000 cc. of both solutions, a certain percentage, about equal in the two instances, remains in the circulation, whereas of the additional doses a much smaller, again about equal, percentage stays in the blood stream. This partial exhaustion of the process of hemodilution is possibly due to an escape of the macromolecular substance from the circulation after it has reached a threshold. Investigations by others on gelatin [16] and by our group [17] on pectin have revealed that both substances are excreted in the urine relatively soon after administration and, furthermore, that the plasma level is decreased greatly at a time when the hemodilution is still maintained. These findings could be explained by the assumption that the macromolecular substance, which starts the hemodilution, leaves the circulation and is substituted by something else which maintains it, at least partly. The labile plasma proteins which potentially enter the circulation are possibly responsible for this mechanism.[18] This would agree with the presented experiences in which hemodilution following the administration of large doses was less severe in patients with anemia or hypoproteinemia, for whom an exhaustion of the labile protein depots could be assumed. If this concept is right, the presence of the macromolecular substance, independent of its nature, elicits a response which could be called an autotransfusion with plasma proteins and which is possibly part of the hematologic reaction of Hueper.[3]

The increase in the sedimentation rate, which is an index of the pseudoagglutination of the red cells and which was selected as an example of the hematologic changes, is of the same degree in both instances and again levels off with the administration of higher doses. Whether the increase of the sedimentation rate is of practical significance is sub judice; however, there is no difference between the sedimentation rate following administration of gelatin and that following administration of pectin.

16. Parkins and others.[7f] Little and Dameron.[7h]

17. Kozoll, D. D.; Volk, B. W.; Stiegmann, F., and Popper, H.: Pectin Excretion in Humans, to be published.

18. Taylor and Moorhouse.[6b] Parkins and others.[7f]

The two substances differ decisively, however, in the production of changes in the tissues. Gelatin causes only a transient vacuolation of the proximal convoluted tubules in the kidney. Chemical identification of these droplets was not possible; however, one can assume that they were due to reabsorbed gelatin which attracted water and caused the hydropic swelling, which morphologically simulates that produced by sucrose.[19]

The dilatation of the renal tubules and glomerular spaces after administration of pectin, a transient sign of forced diuresis, is probably insignificant; not so, however, is the deposition of a peculiar material in spleen, liver and kidneys, which somewhat resembles amyloidosis. Since the spleen is enlarged after administration of pectin, much of the material is apparently deposited in the spleen. The deposition may start in the capillaries, where it may be concentrated as in the glomeruli, where blood is concentrated, or in the lung. It may penetrate into the tissue spaces and may fill them completely, as in the pulp of the spleen or the portal triads of the liver. It often appears concentrated in tissue spaces, and the impression is gained that it is precipitated around reticulum fibers which it infiltrates. It is also taken up by Kupffer cells of the liver, reticuloendothelial cells of the spleen, glomerular cells of the kidney and alveolar cells of the lung. The material is an irritant which causes severe reaction of the reticuloendothelial cells and hyalinization of renal glomeruli.

The nature of the material is not established. The selective staining with ruthenium red suggests pectin. However, the specificity of the ruthenium red reaction in tissues deserves further investigation. It is possibly a polymerization product of pectin with a higher molecular weight than that of the injected pectin.[5a] The staining with dyes which do not stain pectin suggests an admixture of other substances, possibly of protein nature.

Whatever the nature of the material, it is related to retention of pectin in the tissues, more so since similar pictures were produced by administration of pectin to animals by Hueper and ourselves. The difference between pectin and gelatin is not surprising, since there is more reason to suspect in tissue cells the presence of enzymes more capable of splitting gelatin than pectin.

19. Anderson, W. A. D., and Bethea, W. R., Jr.: Renal Lesions Following Administration of Hypertonic Solutions of Sucrose: Report of Six Cases, J. A. M. A. **114**:1983 (May 18) 1940.

How significant is the deposition of pectin in organs? The histologic picture does not exclude the possibility that the uremia in the 2 patients with nephrosis who had received pectin solution was due to the deposition of the peculiar material in the glomeruli. However, the amounts of pectin solution which produced the reported changes are far in excess of those given to patients in shock. We do not know whether other pectin solutions, which are subjected to prolonged autoclaving and are of smaller molecular weight, produce the same changes. Hartman [20] has informed us that in similar studies on human beings and animals his pectin solutions failed to produce changes comparable to ours. He stated that our pectin solutions were prepared by a method subsequently modified by him. We are aware that the physicochemical nature of a given macromolecular solution is of great significance. In addition, it should be stressed that with quantities ordinarily used in the treatment of shock such changes in the tissues have not been observed.

As regards the solutions used by us, despite equal physiologic and therapeutic efficiency, gelatin deserves preference over pectin as a substitute for plasma in the treatment of shock in view of possible changes in the tissues. If the need for a substitute for plasma of nonhuman origin should arise for an autotransfusion of plasma proteins, gelatin should first be considered because of less tissue reaction.

20. Hartman, F. W.: Personal communication to the authors.

SUMMARY

Experiences with administration of gelatin and pectin solutions—which were used as substitutes for plasma in the treatment of shock— to a series of 317 patients in shock and not in shock were compared. The two solutions produce an equal degree of hemodilution which levels off with administration of higher doses of both solutions. This leveling off is more pronounced in patients with anemia and hypoproteinemia. The hypothesis is suggested that the hemodilution is started by the macromolecular solution but maintained by other substances, possibly labile plasma proteins. Gelatin and pectin solutions produce an equal rise in the sedimentation rate, which is considered an index of hematologic changes. The significant difference between the two solutions lies in the fact that gelatin produces less change in the tissues whereas after administration of amounts of pectin in excess of those used for patients in shock splenomegaly and deposition of a peculiar material in various organs may be observed. The material is selectively stained by ruthenium red, a dye used for staining pectin. It is found in phagocytic cells, capillaries, tissue spaces and infiltrating reticulum fibers in the spleen, kidneys, liver and lungs; it resembles deposits of amyloid and causes a reaction of the reticuloendothelial cells. A similar picture was produced in animals by administration of large amounts of pectin. The clinical significance of these changes is admittedly unknown. Since the beneficial effects of gelatin and pectin appear equal on the basis of changes in the tissues, gelatin appears preferable to pectin in the form used.

MALIGNANT RENAL NEOPLASMS

A CLINICAL AND PATHOLOGIC STUDY

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Aware of recent pessimistic expressions made by various authors concerning the prognosis for malignant renal neoplasms, we undertook this study in order to evaluate our diagnostic methods and also to determine the possible clinical and pathologic factors which influence the prognosis and are conducive to a higher survival rate. We have collated the data on 63 consecutive malignant renal neoplasms. Of the 63, 53 were confirmed by operation and 10 by necropsy. We have omitted data on all benign tumors of the parenchyma, pelvis and capsule.

PATHOLOGY

In reviewing the literature one finds numerous classifications of renal neoplasms, many of which are complicated and presented with lengthy arguments in their support. We have adopted a rather simple classification, which is presented in table 1, and which we feel combines the important histologic features with the anatomic site of origin of these neoplasms.

TABLE 1.—*Classification of Sixty-Three Malignant Renal Neoplasms*

	No. of Cases	
I. Malignant tumors of the parenchyma		
A. Hypernephroma (Grawitz)	48	(76.19%)
B. Adenocarcinoma		
1. Tubular	5	(7.94%)
2. Papillary	1	(1.58%)
C. Wilms tumor	3	(4.76%)
II. Malignant tumors of the mucosa of the pelvis or calices		
A. Transitional cell carcinoma		
1. Infiltrating	3	(4.76%)
2. Papillary	2	(3.19%)
B. Squamous cell carcinoma	1	(1.58%)
Total	63	

Hypernephroma.—The most frequent type of malignant tumor observed in our series was the so-called hypernephroma. Because of the small number studied we do not feel justified in attempting to draw any far reaching conclusions as to the histogenesis of the malignant Grawitz tumor. We are inclined to favor the view that this type of tumor is derived from nephrogenic tissue. In support of this theory we found that in our group of 48 hypernephromas 25 of the tumors (52 per cent) were located in the middle or lower thirds of the kidney. However, we were unable to find deposition of hyaline droplets in the large polyhedral cells which line the pseudolumens, as has been described by some proponents of this theory.[1]

The hypernephromas in our series were round or globular in shape, with an irregular or nodular surface. The cut surface possessed a rich yellow color with interspersed areas of hemorrhage, necrosis and fibrosis. Small deposits of calcium salts within the tumor mass were frequently observed. Although the tumor was usually well demarcated from the surrounding parenchyma, a distinct fibrous capsule could not be demonstrated in many cases. Many of the tumors showed considerable variation in the cellular structure. The characteristic polyhedral clear or foam cell with its small pyknotic nucleus predominated, but variations in the size, formation and arrangement of the cells and their nuclei were frequently found in the same tumor. In several cases tumor giant cells were seen. Mitoses were not infrequent accompaniments of these histologic variations. In several cases, cells with a granular cytoplasm were found in isolated areas or in close proximity to predominant groups of clear cells. In no instance were granular cells the sole or prominent cellular element. Consequently we did not attach much significance to cytoplasmic changes as a differential diagnostic feature in dividing malignant Grawitz tumors into various histologic types.

In the group of 48 malignant Grawitz tumors there were 2 specimens in which malignant degeneration was observed in the walls of a solitary cyst. Two neoplasms were found in congenital anomalous kidneys, i. e., in the right half of a horseshoe kidney and in the lower half of a double left kidney.

From the Departments of Urology and Pathology, Sinai Hospital.

Read before the Section on Pathology and Physiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Schiller, W.: Histogenesis of So-Called Grawitz Tumor, Arch. Path. **33**:879 (June) 1942.

Adenocarcinoma.—We have restricted the use of the term adenocarcinoma to a relatively infrequent group of tumors which exhibit distinct tubular or papillary cellular arrangements. On gross examination these tumors show little or no features which distinguish them from malignant Grawitz tumors, and they are not limited to any one portion of the kidney. Microscopic study showed considerable variation in the cellular structure. In several cases, the tumor was composed of fine strands of cells of a uniform low columnar nature, which were arranged in either tubular or papillary fashion. Mitotic figures were absent or rare. In 1 case, the tubules of the kidney were reproduced on a large scale and the individual cells were of unusually large size, arranged in concentric fashion with a central lumen and ensconced in a thin fibrous network. The cytoplasm was granular and in some instances vacuolated. An occasional cell was multinucleated.

Adenocarcinomas are apparently derived from the tubules of the kidney and probably represent adenomas which have undergone malignant changes.

It is noteworthy that the apparent gross encapsulation of the tumor mass in cases of hypernephroma and adenocarcinoma was found on microscopic examination to be distinctly incomplete. In many areas the tumor tissue appeared to be in direct contiguity with the compressed but intact renal parenchyma. In those cases in which a true tumor capsule did exist, it was composed of a dense but not very broad layer of connective tissue which was frequently invaded by tumor tissue.

Wilms Tumor.—The group of Wilms tumors was small (3 cases). All 3 cases came to necropsy at the Sinai Hospital. In 1 case, a woman aged 23 years had had the primary tumor of the left kidney removed elsewhere, where it was diagnosed as an embryonal carcinoma of the Wilms type. The histologic character of the locally recurrent tumor mass was readily discernible, as the patient had not received irradiation before or after operation. In the other 2 cases extensive irradiation before and after operation had been employed and had resulted in marked distortion of the microscopic picture.

The gross specimens of the 2 primary Wilms tumors which came under our direct observation were distinctly dissimilar. In 1 neoplasm was situated in the middle third of the kidney and on cross section presented a light brown bulging surface, which was fairly well demarcated from the surrounding parenchyma. The other specimen presented a most unusual appearance. Although the tumor arose in the middle third of the kidney, it extended outward and upward along the medial surface, capping the upper pole of the kidney and forming a larger extrarenal than intrarenal mass. The cut surface of the tumor showed extensive hemorrhage and necrosis resulting from intensive irradiation.

Malignant Neoplasms of the Mucosa of the Pelvis and the Calices.—The relatively high incidence of the pelvic type of tumor, i. e. 6 cases (9.5 per cent), in our small series was striking. We encountered 5 neoplasms of the transitional cell variety (i. e. 3 infiltrating and 2 papillary) and 1 squamous cell carcinoma. The transitional cell carcinomas were fairly extensive growths which were not encapsulated and in the fresh state closely resembled grossly a Grawitz tumor; their true nature was revealed only on microscopic examination. Microscopically they showed a tendency to spread through the kidney in strandlike fashion with considerable fibrous reaction. In some areas they grew in broad sheets in a manner similar to that of Grawitz tumors. Strands of tumor cells were easily discernible within lymphatics and blood vessels. On the other hand, the 2 transitional cell carcinomas of the papillary type presented purely superficial growths, of which 1 extended down and involved the entire ureter and the other was localized to the lower half of the pelvis with projection into the upper third of the ureter. Associated with the latter growth was a distinct hydronephrotic process in the upper half of the kidney. In both transitional cell carcinomas the papillary folds were shallow and thin and microscopically closely resembled the fronds of vesicle tumors.

The single squamous cell carcinoma in our series was in a kidney which had had ligation of the pedicle some months before extirpation and when inspected was so distorted that any attempt to describe a picture which might be characteristic for a neoplasm of this cell type was nullified. Nevertheless, obliteration of a lower calix by a firm whitish tumor mass could be made out. Microscopically, the characteristic large polyhedral cells with intercellular bridges were evident and mitotic figures were numerous. The absence of true sarcoma of kidney in this small series is not unusual in view of the rarity of this tumor.

Metastases.—It is regrettable that the data concerning metastases are available for only 13 of the 48 malignant Grawitz tumors. In this small series the lungs were involved most frequently (7 cases). The bones and the liver were next (6 cases each). Other organs and structures involved were the regional lymph nodes (5), the

spleen (4), the adrenal glands (3), the opposite kidney (2), the heart (2), the brain (2) and the seminal vesicle (1). There was a local recurrence in the operative area in 2 cases. These data are in accord with the reports of other authors.

The series of neoplasms classified as adenocarcinoma, Wilms tumor and tumor of the pelvis were too small for statistical analysis. However, the most widespread distribution of metastases in our series occurred with squamous cell carcinoma of the renal pelvis.

ASSOCIATED PATHOLOGIC CONDITIONS

It is not uncommon for renal tumors to be accompanied by other lesions within the urinary tract or by disease involving other organs or systems. Associated lesions were present in 21 (33.3 per cent) of the 63 cases. The most common lesions were of the cardiac type, i. e. hypertensive heart disease (10 cases), arteriosclerotic heart disease (8 cases) and coronary heart disease (2 cases). Renal lesions were present in 14 cases, i. e. calculi in 5 cases, acute pyelonephritis in 2 cases and solitary cyst in 2 cases. Prostatic lesions were noted in 13 cases, i. e. benign hypertrophy (7 cases), median bar (4 cases) and calculi (2 cases). Lesions of the bladder were found in 3 cases, i. e. carcinoma in 2 cases and calculi in 1 case. Diabetes was present in 4 cases, syphilis in 2 cases, asymptomatic varicocele in 1 case and carcinoma of the large bowel in 1 case.

The relatively high incidence of renal calculi associated with renal tumors was rather impressive and in accord with the observations of other authors. Five malignant Grawitz tumors were associated with renal calculi (8 per cent). The preoperative symptoms of 3 were attributed to the calculi, and the tumors were detected at operation. Two tumors were diagnosed as solitary cysts on the basis of urographic findings and confirmed at operation; but when the cysts were opened at the operating table suspicious tumor tissue was found in the walls of the cysts, and the kidneys were removed.

One of the most striking observations in our study was the high incidence of multiple primary tumors. There were 5 of this type. Bilateral primary malignant Grawitz tumors were present in 1 case.

AGE INCIDENCE

Our findings are in accord with the reports of other authors. The hypernephromas were encountered most frequently in the sixth decade (30 cases) and in the seventh decade (12 cases). The oldest patient with a hypernephroma was 68 and the youngest 23. The 5 patients with tubular adenocarcinoma were 51, 52, 55, 58 and 62 years of age respectively. The patient with the papillary adenocarcinoma was 25 years of age. The Wilms tumors were observed in 2 children, 3½ and 8 years old respectively, and in 1 adult, aged 23. The oldest patient was 71 years of age and had a transitional cell carcinoma of the pelvis of the kidney.

SEX INCIDENCE

The neoplasms in our series involved 35 males and 28 females. The 48 Grawitz tumors occurred in 27 men and 21 women. There were 2 men and 3 women with tubular adenocarcinoma. The 1 papillary adenocarcinoma occurred in a woman. The 6 carcinomas of the renal pelvis occurred exclusively in males. The 3 Wilms tumors occurred in females. The 5 renal tumors observed in patients below the age of 25 years occurred in females.

KIDNEY INVOLVED

The various types of renal tumor exhibit no selective affinity for one kidney. In our series 31 neoplasms involved the right kidney and 31 the left; in 1 case there was bilateral involvement.

SYMPTOMS AND CLINICAL SIGNS

A careful study was made of the initial symptoms and their duration in order to determine their diagnostic and prognostic significance.

The most common initial symptom was hematuria, the next was pain and the least common a tumor mass. Hematuria was the chief complaint in 22 cases (35 per cent) and was combined with pain or mass or both in 11 additional cases (52 per cent). Pain was the initial symptom in 16 cases (25 per cent) and was accompanied by hematuria or a mass or both in 14 other cases (47 per cent). A palpable mass was the initial symptom in only 2 cases (3 per cent) but was associated with hematuria or pain or both in 9 cases (17 per cent).

We found that the duration of symptoms is extremely variable and that it is extremely difficult to estimate the average time which elapses between the appearance of the first symptoms and the institution of treatment. In 16 cases the symptoms were present for less than one month, and in 30 cases symptoms were present from one to twelve months. We were surprised to note the high percentage of cases in which symptoms lasted from one to seven years and attribute this deplorable situation to negligence on the part of the patient or procrastination on the part of the physician.

Our experience has been that the nature and duration of the initial symptoms have little diagnostic or prognostic significance. However, the necessity for early recognition of and immediate attention to these early symptoms is obvious. It is unfortunate that frequently too great an interval elapses before the initial hematuria appears or the tumor becomes palpable and by this time the condition has advanced to an inoperable stage, precluding the possibility of a cure. On the other hand, the initial hematuria may serve merely as a warning of the presence of a serious but not hopeless condition.

Hematuria.—Hematuria was the most striking symptom in our series. It was observed in 51 cases (81 per cent), being macroscopic in 38 cases (60 per cent), microscopic in 13 cases (21 per cent) and absent entirely in 12 cases (19 per cent). In 5 cases gross hematuria was a relatively late symptom, occurring weeks or months after the initial symptoms of pain or a mass. Not infrequently the hematuria was painless, lasted such a short time and occurred so long before the other symptoms presented themselves that both the patient and the physician disregarded its importance and were lulled into a false sense of security. In our experience the hematuria was rarely of sufficient intensity or amount to immediately endanger the life of the patient, although hematuria of such intensity has been reported. Hematuria must be regarded as an unfavorable prognostic sign, since its presence is dependent on invasion and ulceration of the mucosa of the pelvis or the calices by the neoplasm.

Pain.—Pain was the most frequent symptom in our series. It was present at some time or other during the course of the disease in 59 cases (94 per cent). The nature of the pain varied considerably. In a few cases, the pain was associated with hematuria and was due to the passage of long stringy clots, which occluded the ureter and caused distention of the pelvis. In most cases it occurred independently of hematuria or other symptoms and often preceded these symptoms by months or years. In such cases, the pain was spontaneous, intermittent or constant and was described by the patient as being of a dull "neuralgic" or "colicky" nature. The pain is usually localized to the lumbar region or to the overlying upper abdominal quadrants. In rare instances it may radiate along the distribution of the iliac, inguinal or genitocrural nerves and be referred to the lumbosacral joint, hips, thighs or knees. This occurred in 4 of our cases. In a few cases the pain was referred to the epigastrium or lower abdominal quadrants and was attributed to displacement and pressure on adjacent organs by the tumor mass or to reflex irritation of these organs.

Tumor Mass.—A palpable tumor mass was noted in 40 cases (63.4 per cent) but was the chief complaint in only 2 cases (3.1 per cent). The frequency with which a tumor mass is detected is dependent to a considerable extent on the skill of the examining physician. Since renal tumors vary in size, shape, position and consistency, certain tumors cannot be palpated or can easily be overlooked.

Other Clinical Manifestations.—We were also impressed with the incidence of other clinical signs and symptoms associated with renal tumors.

1. Localized tenderness over the tumor, anteriorly or posteriorly, was present in 22 cases (34 per cent).

2. Loss of weight and strength was reported in 47 cases (74.4 per cent). Cachexia was observed as a late manifestation in 7 cases of advanced tumor (11 per cent), in which there were other outstanding symptoms of many months' duration.

3. Temperature varying between 101 and 103 F. and unaccompanied by evidence of infection in the urinary tract was present in 13 cases (21 per cent). The significance of hyperpyrexia in these cases is not clear, but it is presumably related to necrosis or hemorrhage within the tumor or to the liberation of toxic products by the tumor. In 3 additional cases the temperature was as high as 104.5 F., but this was accompanied by pyuria associated with pyonephrosis in 2 cases and with perinephritic abscess in 1 case.

4. Symptomatic varicocele (Guyon's sign) was observed in only 1 case (1.5 per cent); this occurred in a man aged 71 years who had a transitional cell carcinoma of the left renal pelvis and an adenocarcinoma of the sigmoid.

5. Urinary symptoms, i. e. urgency, frequency, nocturia, dysuria and burning, were reported in 16 cases (25 per cent) and were either associated with lesions of the prostate gland and bladder or accompanied by pyuria which was caused by infectious lesions of the kidney.

6. Gastrointestinal symptoms, i. e. nausea, vomiting, distention, eructation, vague abdominal pain and constipation, were observed in 11 cases (17.4 per cent).

7. Hypertension was observed in 11 cases (17.4 per cent). In 9 adults the preoperative blood pressure exceeded 160 systolic and 90 diastolic and after operation it dropped con-

siderably but soon rose to the preoperative or to a higher level in all but 2 of the patients. The blood pressure was 142 systolic and 84 diastolic in the 8 year old girl with a Wilms tumor and was not influenced by operation.

8. A slight or moderate degree of anemia was noted in the majority of cases, but a severe degree of anemia was present in only 9 cases (14.5 per cent).

The combined clinical triad of hematuria, pain and tumor mass was the chief symptom in 2 cases of advanced tumor and was noted in 21 cases during the course of the disease. These observations indicate the relatively infrequent occurrence and diagnostic unreliability of this combined triad in cases of renal tumor. In our experience the presence of this triad usually signified a far advanced and often hopeless condition.

In Wilms tumors in infants and in advanced or inoperable conditions in adults, the symptom triad may be reversed, i. e. a palpable mass and pain may exist for an indefinite period without hematuria.

Experience has shown that in order to establish early diagnosis it would be better to place less emphasis on this clinical triad and impress on the members of the medical profession and on the patients the serious import of blood in the urine, which should demand a thorough urologic study.

DIAGNOSTIC PROCEDURES

While the aforementioned signs and symptoms, as determined by a careful history and physical examination, have proved to be invaluable aids in the diagnosis of renal tumors, equally important is the information obtained by special urologic examinations, viz.: (1) urinalysis, (2) tests of renal function, (3) cystoscopy and (4) roentgenographic studies.

Examination of Urine.—A careful analysis of the urine should be done in every case of suspected renal tumor. The frequent occurrence of microscopic hematuria in our series is an indication of its diagnostic importance. The following urinary abnormalities were noted: microscopic hematuria (13 cases), gross pyuria (3 cases), microscopic red blood cells and pus cells (15 cases) and albuminuria (4 cases).

Tests of Renal Function.—We place greater reliance on phenolsulfonphthalein than on indigo carmine as a test of combined renal function. A phenolsulfonphthalein test and determination of the blood urea are done routinely on the patient's admission to the hospital.

Cystoscopic Study.—A complete cystoscopic examination is an indispensable aid in the diagnosis of renal tumors. The study should be performed with the patient under intravenous or spinal anesthesia in order to allay his fear of pain. One cannot emphasize too strongly to the laity and to the members of the medical profession the importance and necessity of performing a cystoscopic study during the period of active renal bleeding. The evil consequence of delaying examination until the hematuria has ceased enhances the diagnostic difficulties and militates against the possibility of a cure through an early diagnosis and operation.

Careful inspection of the bladder during the period of active bleeding enables the cystoscopist to determine the exact source of the bleeding and to rule out the presence of benign or malignant lesions of the posterior urethra, the prostate, the vesical neck or the bladder.

A phenolsulfonphthalein test should be performed with each catheter in place. In several cases we found considerable diminution of function in the affected kidney, and in a few cases function was completely absent.

Roentgenographic Studies.—This procedure is one of the most valuable diagnostic methods at our disposal. A plain film should be taken shortly after the patient's admission to the hospital or at the time of cystoscopy, as it often discloses valuable information concerning alterations in the size and shape of the kidneys as well as irregularities in the outline produced by renal tumors.

In the present study, retrograde pyelography was employed in 56 cases and intravenous urography in 10 cases. No urographic studies were performed in 7 cases, in which a renal tumor was not suspected but was disclosed at necropsy. In our clinic greater reliance is placed on retrograde pyelography than on intravenous urography. It is our contention that the diagnosis of renal tumor made on the basis of intravenous urographic findings is extremely difficult and hazardous in view of the frequent incomplete filling defects noted with this method, which are so confusing and misleading. We prefer to use intravenous urography as a supplement and not as a substitute for retrograde pyelography. Intravenous urography is useful for patients who are toxic or in the late stage of the disease, when cystoscopy and retrograde pyelography are contraindicated.

It is a routine procedure in our clinic to take stereoscopic films with a catheter in each ureter. This enables us to determine the degree of displacement of the ureter and the relation of the ureters to calcified shadows in and about the kidney. Before proceeding to take stereoscopic ureteropyelograms we make an accurate deter-

mination of the renal pelvic capacity by distending each pelvis with measured amounts of sterile distilled water. This will indicate the amount of 20 per cent solution of skiodan sodium to be injected and at the same time give valuable information concerning the nature and location of the pain. We have employed lateral pyelograms in several cases in which the diagnosis was doubtful. When the diagnosis following retrograde pyelography is doubtful because of difficulty of excluding a filling defect or occlusion of the pelvis or calix due to insufficient injection of a pyelographic medium, it is advisable to repeat the pyelographic studies. In such cases we have intentionally overdistended the renal pelvis with 20 per cent solution of skiodan sodium and obtained a sharper delineation of the distorted, elongated or compressed calices and pelvis. We have also observed that with this method the contrast medium never penetrates the encapsulated hypernephroma but does penetrate the adjacent unaffected parenchyma by pyelotubular or pyeloparenchymatous back flow.

An analysis of the urographic findings in the 56 cases in which retrograde pyelography was employed are enumerated below:

	Cases
(a) Compression of one or more calices	53
(b) Elongation of one or more calices	51
(c) Partial or complete obliteration of one or more calices	48
(d) Dilatation of one or more calices	6
(e) Distortion or compression of the pelvis	36
(f) Dilatation of the pelvis	10
(g) Displacement of the pelvis	12
(h) Displacement of the ureter	15
(i) Calcification within the tumor	8
(j) Renal calculi	5

These pyelographic studies were of considerable value in establishing a correct preoperative diagnosis in 42 (75 per cent) of 56 cases in which retrograde pyelography was employed.

Experience has shown that comparatively little information relating to the particular histologic type of neoplasm is obtained from the changes just enumerated. As a rule, changes due to compression, distortion and occlusion in one or more calices accompanied by displacement of the pelvis or ureter occur more frequently with hypernephroma, whereas filling defects of the pelvis are more characteristic of carcinoma of the pelvis.

It is well to remember that there are many renal lesions which may produce one or more of these changes and must be considered in the differential diagnosis. These lesions include: (*a*) spasm of the pelvis, calices or ureter; (*b*) lesions within the pelvis or the calices, i. e. blood, pus, granulomas, cystic dilatations and air bubbles; (*c*) calculi in the pelvis or calices; (*d*) deformities associated with intrarenal obstructive or inflammatory processes, i. e. hydronephrosis, pyelonephritis, pyonephrosis, cortical abscess and perinephritic abscess; (*e*) deformities associated with cystic disease, i. e. solitary cyst and polycystic disease; (*f*) deformities associated with extrarenal or retroperitoneal tumors; (*g*) deformities associated with congenital anomalies; (*h*) deformities associated with acquired ptosis or torsion.

Calcification within the tumor offered some diagnostic difficulty, as occasionally these areas of calcification were confused with renal calculi, calcification due to tuberculosis or calcification within a chronic pyonephrotic kidney. The singularity and the irregular patchy nature of these areas of calcification, which are usually found in necrotic areas near the center of the neoplasm, distinguish them from the multiple areas of fine granular calcification due to tuberculosis and from the sharp outline of renal calculi. The prognostic significance of calcification within renal tumors was also studied. It was found to have a favorable influence on 5 patients with hypernephromas; i. e. 3 patients lived sixteen, eleven and eight years respectively after operation and 2 were living and well four and five years respectively after operation. In 2 patients the calcification was associated with a transitional cell carcinoma of the renal pelvis, and these patients died one year and two months respectively following operation. Roentgenographic studies of the lungs and long bones should be employed routinely in every case of suspected renal tumor.

Diagnosis.—The preoperative diagnosis was correct in 41 cases (65 per cent) and incorrect in 18 cases (28.5 per cent); the condition was unsuspected but diagnosed at autopsy in 4 cases (6.5 per cent).

An analysis of the 18 cases in which an incorrect preoperative diagnosis was made is presented in table 2.

TABLE 2.—*Analysis of Eighteen Cases in Which the Preoperative Diagnosis Was Incorrect*

	No. of Cases	
(a) Renal calculus	2	(Stones found but tumor unsuspected)
(b) Calculous pyonephrosis	2	
(c) Pyonephrosis	3	
(d) Tuberculosis	3	
(e) Solitary cyst	2	(Cyst found but malignant changes in wall of cyst unsuspected)
(f) Perinephritic abscess	1	(Abscess found; tumor unsuspected)
(g) Chronic nephritis	1	
(h) Ovarian cyst	1	
(i) Splenomegaly	1	
(j) Retroperitoneal tumor	1	
(k) Acute empyema of gallbladder	1	
Total	18	

It is not always possible to distinguish the type of neoplasm present from clinical symptoms of

pain, hematuria and mass and urographic findings. One can, however, be guided by knowledge of the relative frequency and the age incidence of the various types of neoplasm.

TREATMENT

The only hope for the cure of renal neoplasms lies in early and complete removal of the affected kidney before metastases have developed. The feasibility of operative treatment requires the careful consideration of many factors, i. e. the condition of the patient, the nature and duration of symptoms, the size and mobility of the tumor and the presence of metastases. Each case presents a distinctly different problem, which may tax the skill and judgment of the urologist. Not infrequently seemingly hopeless patients are restored to apparent good health and economic usefulness after nephrectomy. Surgical treatment is also indicated in cases in which a doubtful or questionable diagnosis of renal tumor has been made, in order to determine the presence of a benign or a malignant lesion. An exploratory operation is indicated in every case of suspected renal neoplasm.

There is no unanimity concerning the advisability of operative treatment in the presence of metastases. It is generally agreed that surgical intervention is contraindicated in cases of multiple or disseminated metastases. There is some difference of opinion concerning surgical operation for patients with solitary asymptomatic metastasis in the lungs or the bones. In 1 of our cases, the right half of a horseshoe kidney containing a hypernephroma was removed because of severe bleeding and pain despite the presence of several isolated metastatic nodules in the lungs. The patient lived for eight months after operation.

There are two accepted avenues of approach for the removal of renal tumors, viz., lumbar and transperitoneal. It is generally agreed that the lumbar route is preferable for small or moderate-sized hypernephromas and for carcinomas of the pelvis. The lumbar route is also indicated when the diagnosis is uncertain. The transperitoneal approach is best suited for large and firmly fixed tumors, i. e. large Grawitz tumors, adenocarcinomas and Wilms tumors. The lumbar route also suffices in those cases in which irradiation has been employed preoperatively to shrink the tumor.

With the Wilms tumor, adenocarcinoma and squamous or transitional cell carcinoma of the pelvis, it is advisable to remove as much of the perinephritic adipose tissue as possible together with the kidney. For papillary carcinoma of the renal pelvis, a complete nephroureterectomy, including excision of a small segment of the vesical wall, should be performed in one or two stages.

We wish to emphasize the importance of exposing the vascular pedicle as early as possible, preferably before freeing or delivering the kidney. This enables the surgeon to examine the renal vein and the inferior vena cava for tumor thrombi and to remove them if present. It also permits ligation of the vascular pedicle before mobilizing the kidney. This precautionary measure prevents the dislodging of tumor thrombi into the renal vein or the squeezing or liberation of tumor cells into the general circulation, as a result of the forcible manipulation incidental to the exposure and delivery of the kidney. In 2 cases in the present study tumor thrombi were deliberately removed from the renal vein and in 1 case from the inferior vena cava before ligation of the pedicle. In all 3 cases the patient survived the operation for two years or more and failed to show evidence of metastases following operation. Care must also be exercised to insure complete removal of the growth without rupturing the tumor. The escape of tumor cells into the perirenal tissue is usually responsible for a recurrence in the operative area or in the incision.

The operability of a renal tumor should be based on the following features: (1) penetration of the tumor through its capsule; (2) presence of perirenal tumor infiltration; (3) abnormal fixation of the tumor in the renal bed; (4) presence of secondary metastatic deposits in the perirenal and juxta-aortic lymph nodes and the intra-abdominal organs, and (5) presence of tumor thrombi in the renal vein and the inferior vena cava.

Roentgen Therapy.—Our personal experience with irradiation therapy has been extremely limited. Postoperative irradiation was employed in only 2 cases of hypernephroma, with no improvement or benefit. Preoperative and postoperative irradiation was employed in 2 cases of Wilms tumor in children. In the latter 2 cases the growth was extremely large and preoperative irradiation resulted in considerable reduction in the size of the growth and greatly facilitated removal of the tumor. Despite extensive postoperative irradiation, both children succumbed from regional extension and metastases within two years after operation.

OPERATIVE MORTALITY

One of the most outstanding achievements of surgical treatment on the genitourinary tract in

the past thirty-five years has been the great reduction in operative mortality following nephrectomy for renal tumors. This accomplishment is due partly to the refinements in surgical technic and improvements in anesthesia and partly to the more careful selection and preparation of patients for operation.

There has been a gradual reduction in the operative mortality from 30 (Garceau) to 50 per cent (Squier [2]) in the early period of renal surgery to 1.2 (Priestley [3]) to 2.8 per cent (O'Conor [4]).

Fifty-three of the neoplasms in our series were treated by nephrectomy, with 4 operative deaths (7.5 per cent). The operations included 6 transperitoneal nephrectomies, with no deaths, and 47 lumbar nephrectomies, with 4 deaths (8.5 per cent). The cause of death was shock in 3 cases, fourteen occurring twenty-four and forty-eight hours postoperatively respectively, and cardiac failure with hemiplegia in 1 case, occurring on the fourteenth postoperative day. An exploratory operation was performed in 5 cases, with 2 deaths (40 per cent); 1 death due to uremia and 1 due to cardiac failure occurred on the fourth postoperative day.

More than 50 per cent of the 53 nephrectomies were performed by the two attending urologists of the service (Dr. Goldstein—21; Dr. Abeshouse—12). The remaining 20 operations were performed by eleven members of the general surgical and gynecologic staffs.

SURVIVAL RATE

Despite the remarkable reduction in the operative mortality achieved in the past thirty-five years, the survival rate has not been appreciably increased in the same period. Consequently some writers have adopted a pessimistic attitude toward the value of operative treatment, particularly for parenchymal neoplasm and infiltrating type of carcinoma of the renal pelvis. The increasingly good results obtained following complete nephroureterectomy in cases of papillary carcinoma should help to overcome this defeatist attitude.

Of the 53 patients treated by nephrectomy, data concerning the length of life after operation were available on 44 of them; there were no available data on 5 of the patients, and there were 4 postoperative deaths.

Analysis of the data on survival for 34 of the patients with Grawitz tumors reveals:

	No. of Cases	Per Cent
I. Length of life following operation		
(a) Death within 1 year	5	14
(b) Death within 2 years	10	29
(c) Survival 3 years or more	11	32
(d) Survival 5 years or more	7	20
(e) Survival 10 years or more	5	14
(f) Survival 15 years or more	2	5
II. Living and well after operation		
(a) Living and well 4 years or more	18	23
(b) Living and well 5 years or more	5	14
(c) Living and well 10 years or more	2	5
III. Cures in terms of years		
(a) 3 year cures	11	32
(b) 5 year cures	12	35
(c) 10 year cures	7	20
(d) 15 year cures	2	5

Three patients with adenocarcinoma were alive and well one, three and five years respectively after operation. One patient with transitional cell carcinoma of the pelvis died within thirteen months, and 1 with squamous cell carcinoma died within two months. One patient with papillary carcinoma of the pelvis was alive and well five months after operation, and 1 died eighteen months after operation. All 3 patients with Wilms tumors were dead within two years.

PROGNOSIS

Much has been written concerning the various factors which influence the prognosis of renal tumors. These factors include: (1) nature and duration of symptoms, (2) general condition of the patient, (3) type, size and mobility of the tumor, (4) tumor thrombi in the renal vein, (5) metastases, (6) surgical treatment and (7) irradiation therapy.

The prognostic significance of the various clinical signs and symptoms has already been discussed. The general condition of the patient is an indication of the degree of malignancy. Slow-growing tumors which usually are of low grade malignancy have little effect on the general constitution. A rapidly growing tumor indicates a high grade of malignancy and may be accompanied by severe toxemia, anemia, loss of weight, fever and cachexia in a manner similar to that of a tumor of high grade malignancy elsewhere in the body.

Broders, Braasch and Griffin [5] and their associates at the Mayo Clinic have repeatedly stressed the prognostic significance of the degree of cellular differentiation in cases of hypernephroma. They maintained that the length of life after operation was considerably longer in cases of tumor with lower grades of malignancy. They

2. Squier, J. B.: Boston M. & S. J. **161**:547, 1909.

3. Priestley, J. T.: Survival Following Removal of Malignant Renal Neoplasms, J. A. M. A. **113**:902 (Sept. 2) 1939.

4. O'Conor, V. J.: South. M. J. **34**:27, 1941.

5. Braasch, W. F., and Griffin, M.: Prognosis in Renal Carcinoma and Clinical and Pathologic Data Affecting It, J. A. M. A. **106**:1343 (April 18) 1936.

also maintained that the duration of preoperative symptoms was longer for tumors with lower grades of malignancy and that the duration diminished as the malignancy increased. Unfortunately too many pathologists have had inadequate experience or have failed to adopt Broders' gradation of malignant neoplasms, which is based on variation in morphologic characteristics, arrangement of cells and manner of growth. Consequently relatively few reports are available to substantiate the prognostic significance of cellular changes. Our personal experience with this method has not been satisfactory. We attempted to correlate the grading of tumors with the survival rate for our group of 48 Grawitz tumors. The majority of these tumors belonged to grades 1 and 2. Several were of grade 3, and only 1 belonged to grade 4 (Broders' classification). The duration of life was so extremely variable with tumors of the first three grades that we were unable to establish any definite relation between these factors or draw any definite conclusions.

The size or weight of the growth is no true indication of the degree of malignancy. It has been our and other authors' experience that small tumors may metastasize as quickly and extensively as larger ones. Generally speaking, the prognosis is better with small movable tumors than with large fixed tumors. The degree of fixation of the tumor is of greater prognostic significance than the size and weight. A firmly fixed tumor usually indicates perirenal adhesions or tumor infiltration, which seriously interferes with mobilization and delivery of the renal tumor and increases the likelihood of dissemination of tumor thrombi or cells. Involvement of the renal vein is not always a fatal sign but certainly decreases the chance of a cure.

The prognosis varies considerably with the different types of neoplasms. Hypernephromas appear to progress slowly at the onset up to a certain point, after which the virulence of the condition increases and the clinical course is rapidly downhill. In our experience the prognosis for hypernephromas was by no means entirely satisfactory, as a large percentage of the patients died within two years of operation, and death was usually caused by metastases and occasionally by local recurrence. The majority of recurrences were within two or three years after the operation.

Our experience with the other renal tumors has been too limited to wararnt personal conclusions. However, a review of the literature reveals uniformly poor results for squamous and transitional cell carcinoma of the renal pelvis. The outlook in cases of papillary carcinoma of the renal pelvis has improved considerably in the past few years, owing to the adoption of complete nephroureterectomy, which insures complete removal of the kidney, the ureter and a small portion of the adjacent vesical wall. The prognosis for Wilms tumor is far from satisfactory, despite the use of preoperative and postoperative irradiation. Better results may be hoped for in the future, due to improvements and refinements in irradiation and operative technics.

CONCLUSIONS

A careful analytic study of 63 renal neoplasms observed in the past twenty years and a review of the literature warrant the following conclusions:

1. Renal neoplasms are more common in men than in women (5:4).

2. These neoplasms occur with equal frequency in each kidney.

3. Parenchymal renal neoplasms are observed most frequently in the sixth and seventh decades of life with the exception of Wilms tumors, which are observed in infancy and early childhood.

4. The most common initial symptom in our series was painless hematuria. Next in frequency were pain and a tumor mass.

5. The classic symptom triad, which may be observed at any time during the course of the disease, is found in the following order of frequency: (*a*) pain 94 per cent, (*b*) hematuria 81 per cent and (*c*) tumor mass 63 per cent.

6. This symptom triad is usually reversed in children with Wilms tumors and in inoperable adults, in whom a mass is usually the presenting symptom.

7. Retrograde pyelographic studies were performed in 56 cases, and a correct preoperative diagnosis based on the pyelographic findings was made in 42 cases (75 per cent). In our clinic greater reliance is placed on retrograde pyelography than on intravenous urography in the diagnosis of renal neoplasms.

8. The most common urographic findings associated with malignant neoplasms in order of frequency are (*a*) compression of one or more calices, (*b*) elongation of one or more calices, (*c*) distortion or compression of the pelvis, (*d*) displacement of the ureter or the pelvis, (*e*) dilatation of the pelvis and (*f*) calcification within the tumor.

9. In parenchymal neoplasms the characteristic pyelographic change is compression, elonga-

tion or obliteration of one or more calices. In pelvic tumors a filling defect of the plevis is the most uncommon finding.

10. In our series of 53 neoplasms treated by nephrectomy, there were 4 deaths (7.5 per cent). These deaths occurred after lumbar nephrectomy. This low operative mortality compares favorably with that given in reports in the past forty years.

11. Surgical intervention is justifiable in every case of suspected renal neoplasm, despite the relatively low survival rate. Early diagnosis and operation increase the chance of cure.

12. The following factors influence the prognosis: (*a*) nature and duration of the symptoms, (*b*) condition of the patient, (*c*) type, size and mobility of the tumor, (*d*) tumor thrombi in the renal vein and inferior vena cava, (*e*) metastases, (*f*) type of surgical treatment and (*g*) irradiation therapy.

13. The best results from the standpoint of survival following nephrectomy were obtained with Grawitz tumors, and the poorest results, following operative treatment for pelvic neoplasms.

14. Our results with Grawitz tumors were gratifying when considered from the standpoint of a three year cure (11 cases [32 per cent]), a five year cure (12 cases [35 per cent]), a ten year cure (7 cases [20 per cent]) and a fifteen year cure (2 cases [5 per cent]).

LIGATION OF THE FEMORAL VEIN FOR CHRONIC OCCLUSIVE ARTERIAL DISEASE

A REVIEW OF ONE HUNDRED AND EIGHTEEN LIGATIONS

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NEW YORK

In 1941 Lesser and I [1] reviewed 20 cases in which ligation of the femoral vein was employed in the treatment of chronic occlusive arterial disease of the lower extremities. As suggested in our preliminary report, the encouraging results demanded further evaluation of this procedure. The present report includes 118 ligations of the femoral vein performed on 110 patients. The results are far from spectacular, but the value of this procedure as judged from our experience definitely places it in the armamentarium for the treatment of chronic occlusive arterial disease, along with the many fairly recent procedures that have appeared in the literature. When a chronic disease is confronted, great dependence is placed on palliative measures. Thus, one attempts to alleviate acute symptoms and also to prevent complications or further spread of the disease. Even when life expectancy is definitely short, palliation is attempted for humane reasons alone. These considerations are still further emphasized in the treatment of patients who in practically every instance are in the older age group and in addition have the increased hazards which accompany systemic degenerative lesions. For aged persons with arteriosclerosis with an incompetent peripheral arterial circulation one should employ any measure which may prevent the dreaded complication of gangrene and subsequent amputation, even though the outlook in view of other associated degenerative lesions greatly limits life expectancy. Ligation of the femoral vein would therefore be indicated when lesions on the foot such as ulcer or gangrene have not made their appearance but when arterial insufficiency is in evidence and the prognosis is obvious. Even in those cases in which gangrene is imminent, ligation of the femoral vein has proved of definite value. Since morbidity or mortality is not associated with this procedure and since it is easily and quickly performed with the area under local anesthesia, no objection can be offered to its use. Under the heading of "Surgical Procedures of Therapeutic Value" Herrmann [2] stated:

> In most patients with obliterative disease of the arteries of the extremities, the real clinical problem is whether or not the development of the collateral arterial circulation can keep pace with the added demands for blood which are being made as a result of the progressive vascular occlusion. From the therapeutic standpoint, therefore, two definite problems arise: first, what can be done to stimulate the development of a collateral arterial circulation; and secondly, what can be done to prevent bacteria from attacking the poorly nourished tissues of the extremity during the active and progressive stages of the disease.

The answers to these problems have brought forth a great many surgical palliative procedures,[3] among which is included ligation of a major vein. All of these procedures actually attempt to bring about the ultimate development of collateral vessels, since this is the only means by which improvement can occur. As in other specialized fields of surgery, with proper indications and in selected cases, each procedure has its own merits. This series of ligations of the

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1. Glasser, S. T., and Lesser, A.: Femoral Vein Ligation for Chronic Occlusive Arterial Disease, Am. J. Surg. **52**:100, 1941.

2. Herrmann, L. G.: Passive Vascular Exercises and Conservative Management of Obliterative Arterial Diseases of the Extremities, Philadelphia, J. B. Lippincott Company, 1936, p. 142.

3. Achmatowicz, L.: Resection of Femoral Artery and Vein as Method of Treatment of Gangrene of Lower Extremities Caused by Endarteritis Obliterans, Polska gaz. lek. **13**:424, 1934. Allen, E. V.: Recent Advances in the Medical Treatment of Peripheral Vascular Diseases, J. A. M. A. **113**:2375 (Dec. 30) 1939. Brooks, B., and Johnson, G. S.: Simultaneous Vein Ligation: Experimental and Clinical Study of Therapeutic Venous Occlusion, Ann. Surg. **100**:761, 1934. Federoff, P. A.: Treatment of Spontaneous Gangrene by Oppel-Petroff's Method: Binding Femoral Vein, Vestnik khir. **16**:177, 1929. Fraser, N. D.: The Conservative Treatment of Thromboangiitis Obliterans: A Report of the Results of Ligation of the Femoral Vein in Six Cases, China M. J. **45**:519, 1931. Pemberton, J. de J., and McCaughan, J. M.: Traumatic Lesions of Arteries: Indications for Therapeutic Ligations of Veins, Ann. Surg. **96**:1103, 1932.

femoral vein is, to the best of my knowledge, the only large series reported in which this special procedure has been given sufficient clinical trial.

What physiologic principles are involved subsequent to ligation of the femoral vein? According to Macleod,[4] the hydrostatic pressure in the capillaries is approximately 22 mm. of mercury. At the proximal (arteriolar) end the pressure is 32 mm. of mercury, while the distal (venular) portion has a pressure of 12 mm. However, in chronic occlusive arterial disease the capillary pressure is decreased to almost hydrostatic value. Starting at the heart, the force (pressure) of flow diminishes as the smaller vessels are approached, so that in the capillaries the flow is fairly constant under normal conditions, irrespective of the intermittent changes of pressure which correspond to the cardiac systole and diastole. It would be fair to assume that with an increase in venous pressure caused by ligation of a major vein the tension on the arterial side would increase sufficiently to open up collateral vessels and augment the vascular bed in general. This presupposes the presence of functioning and available collateral vessels for this purpose. In addition, ligation of the femoral vein reduces to some degree any element of vasospasm which may be present, since some interruption in the sympathetic pathway is incidental to the procedure.

Oppel[5] in 1913 noted that in cases of arterial insufficiency elevation of the limb was associated with pallor and ischemic pain while dependency resulted in hyperemia and disappearance of pain. His explanation was, in effect, that in arterial occlusion when gangrene is impending the blood pressure is so low that with the leg in the horizontal position the hydrostatic pressure is sufficient to stop the criculation. In addition, since elevation of the leg normally decreases the femoral venous pressure to almost zero, it would be expected that where the arterial flow is poor this condition would be exaggerated. Furthermore, the decrease in venous pressure would result in a taking up by the veins of collateral arterial blood, which would further embarrass more distal regions of the limb. However, with the limb in the dependent position, the arteries dilate by virtue of the weight of the blood column, and the venous pressure increases. Following this line of reasoning, Oppel[6] favored ligation of the femoral vein. He stated: "Ligation of the vein is beneficial not because the outflow is reduced, but because reduction in the outflow favorably influences the arterial circulation." He predicted beneficial effects from ligation of the femoral vein for threatened senile gangrene, reasoning that an equalization between the arterial and the venous system of the extremity could be obtained by this method, whereby a slowed venous return allowed for better utilization by the arterial portion of the circulation. Oppel was the first to demonstrate experimentally that after ligation of a large artery ligation of its accompanying vein increased the pressure in the artery, and in 1913 he performed the first therapeutic ligation of the femoral vein. The large number of gunshot injuries to major blood vessels in World War I gave further impetus to interest in this procedure. The statistical work of Makins[7] on experiences with gunshot wounds in the war made acceptable the principle of elective ligation of satellite veins at the time of ligation of a main artery, which caused a definite reduction in the incidence of gangrene of the extremities.

In an experimental study on rabbits, Brooks and Martin[8] found that occlusion of the common and external iliac arteries was followed by gangrene in 15 of 21 animals; the same arterial ligation coupled with ligation of the common iliac vein caused gangrene in only 6 of 18 animals. In further experimental studies, Holman[9] elaborated the principle that ligation of the femoral vein proximal to the site of arterial ligation caused an increase in intra-arterial pressure, which was greater than that obtained when ligation of the femoral vein was done at the level of or distal to the site of arterial occlusion. In 1927 Pearse[10] offered the following experimental observations on cats to explain the lessened incidence of gangrene following ligation of both the artery and the vein: (*a*) ligation of the artery alone caused an immediate increase

4. Macleod, J. J. R.: Physiology in Modern Medicine, St. Louis, C. V. Mosby Company, 1938, p. 376-377.

5. Oppel, cited by Brooks, B.: Surgical Applications of Therapeutic Venous Obstruction, Arch. Surg. **19**:1 (July) 1929.

6. Oppel, A.: Ueber die gestaltliche Anpassung der Blutgefässe unter Berücksichtigung der funktionellen Transplantation, Leipzig, H. Engelmann, 1910.

7. Makins, G. H.: On Gunshot Injuries to the Blood Vessels, Founded on Experience Gained in France During the Great War, Bristol, J. Wright & Sons, 1919, p. 251.

8. Brooks, B., and Martin, K. A.: Simultaneous Ligation of Vein and Artery: An Experimental Study, J. A. M. A. **80**:1678 (June 9) 1923.

9. Holman, E.: Surgery of Large Arteries with Report of Ligation of Innominate Artery, for Varicose Aneurism of Subclavian Vessels, Ann. Surg. **85**:173, 1927.

10. Pearse, H. E., Jr.: A New Explanation of Improved Results Following Ligation of Both Artery and Vein, Ann. Surg. **86**:850, 1927.

of intra-arterial pressure; (*b*) ligation of both the artery and the vein caused still greater increase in the immediate arterial pressure; (*c*) the arterial pressures gradually returned to normal at the end of three weeks; (*d*) arteriograms taken at the end of three weeks showed a greatly increased arterial bed, greater when both the artery and the vein were ligated and when the venous ligation was done proximal to the site of arterial ligation (Holman's principle).

Theis,[11] in an early clinical trial of the method, expressed the opinion that concomitant ligation of the vein was valuable for only a temporary period in acute arterial obstruction and had no appreciable effect on chronic arterial diseases in which the gradual progress of the condition had given the collateral bed an opportunity to develop. Van Gorder[12] used ligation of the femoral vein in a small number of cases of thromboangiitis obliterans and obtained immediate relief of pain and cessation of spread of gangrene in 3 of 5 cases, with complete failure in 1 case. The benefits derived from ligation of the vein were attributed to the resulting increase in venous pressure, in residual arterial pressure and in the peripheral arterial circulatory bed. He stated the belief that periarterial sympathectomy performed at the time of ligation had no material effect on the result. At about the same time Brooke[13] in England performed ligation of the femoral vein combined with periarterial sympathectomy for diabetic gangrene of the extremities. He was enthusiastic about the results obtained, noting improved pulsation of vessels, localization and demarcation of the gangrenous process, cessation of spread, relief of pain and an opportunity to amputate at a lower site when amputation became necessary.

Spurrell[14] ligated the artery and vein in the extremities of cats and then made arteriograms to show the opening up of numerous fine collateral vessels, which were most distinct two to three weeks after ligation. In similar experiments conducted on frogs, he observed under direct visualization the immediate opening up of numerous previously inactive small collateral vessels.

Lewis and Grant[15] and Collens and Wilensky[16] stated the opinion that the beneficial effects of venous obstruction on the arterial circulation are due to the hyperemia which results on release of a venous obstruction. The latter writers give this as an argument against ligation of the femoral vein, even though definite increases in pulse volume have been observed experimentally and clinically on the application of a cuff.

In discussing reactive hyperemia, Homans[17] noted that this can also be obtained by the apparatus of Collens and Wilensky which produces intermittent venous compression. In arteriosclerosis, a low hydrostatic pressure is nearly always present, a condition which may be corrected by venous hyperemia, which raises the filtration pressure so that fluids pass from the capillaries to the tissues. In normal limbs, increased venous pressure increases the flow of lymph. He stated:

> The final effect of increased venous pressure, at a therapeutic (subdiastolic) level, is to lower oxygen tension in the tissues, and thereby create an oxygen want, a want which must be satisfied, upon releasing the cuff, by a reactive hyperemia. Venous pressure, in addition to doing what arterial stoppage does, namely, creating in the tissues an oxygen want, raises the pressure in the capillaries while the venous hyperemia is going on and so confers whatever benefits may be received from that act.

Leriche[18] elaborated the theory that ligation of the femoral vein merely caused in effect what could be accomplished as well by periarterial sympathectomy. Studying the mechanism of action of venous ligation in dogs, he found the increase in arterial pressure after ligation to be transient, gradually returning to normal after some minutes, that is, after the venous collateral circulation had been reestablished. He reasoned that immediately after ligation there occurred an arteriolarcapillary stasis, then a peripheral vasoconstriction, with an increase of peripheral arterial pressure, and when the vein was untied a sharp fall in pressure, due to active vasodilatation. Section of the lumbar ganglions did not alter this phenomenon; furthermore, ligation of

11. Theis, F. V.: Ligation of Artery and Concomitant Vein in Operations on Large Blood Vessels, Arch. Surg. **17**:244 (Aug.) 1928.

12. Van Gorder, G. W.: High Vein Ligation in Thromboangiitis Obliterans: Report of Nine Cases, Ann. Surg. **90**:88, 1929.

13. Brooke, R.: Peri-Arterial Sympathectomy with Ligature of the Femoral Vein in Treatment of Diabetic Gangrene, Brit. J. Surg. **15**:286, 1927.

14. Spurrell, W. R.: Experimental Study of Circulatory Changes Following Ligation of Main Artery and Vein to Hind Limb, Guy's Hosp. Rep. **80**:20, 1930.

15. Lewis, T., and Grant, R.: Reactive Hyperaemia in Man, Heart **12**:73, 1925.

16. Collens, W. S., and Wilensky, N. D.: The Use of Intermittent Venous Compression in the Treatment of Peripheral Vascular Disease, Am. Heart J. **11**:705, 1936.

17. Homans, J.: Circulatory Diseases of the Extremities, New York, The Macmillan Company, 1939, pp. 12-15.

18. Leriche, R., and Fontaine, R.: Mechanism of Action of Venous Ligation in Arterial Obliteration, Lyon chir. **27**:602, 1930.

the vein in one extremity caused the same reaction in the other. He found that the desired therapeutic vasodilatation was accomplished in fifteen minutes to one hour, that is, as soon as the arterial pressure was stabilized.

Pearse [19] studied a group of 20 cases of arteriosclerosis and diabetic gangrene in which he performed ligation of the femoral vein and noted the effect of this procedure on (*a*) the amount of pain, (*b*) the course of the gangrene, (*c*) the pulsation of the vessel and (*d*) the postural changes in color. He found that in 50 per cent of the cases there was definite improvement and in 40 per cent amputation was needed in one year after ligation. He concluded that ligation of the femoral vein is indicated in those borderline cases in which there is evidence of severe but not hopeless arterial damage and occlusion and clinical evidence of impending gangrene. McWhorter [20] ligated both the femoral artery and the femoral vein in a small group of cases of thromboangiitis obliterans and stated the belief that the results were beneficial.

Silbert [21] performed ligation of the femoral vein in 16 cases, 8 of which were instances of thromboangiitis obliterans and 8 of arteiosclerosis. Twenty-four hours after operation, he noted a rise in temperature of the limb, a subjective feeling of warmth in the limb, frequently a dramatic relief of pain and slight swelling of the leg with some distention of the superficial veins. He concluded that ligation of the femoral vein had a definite, though limited value in the treatment of chronic occlusive arterial diseases.

Wilson [22] in England repeated some of the experiments on animals that had previously been performed dealing with venous ligation in cases of arterial occlusion and disagreed with the impressions derived by other investigators. His conclusions were as follows: 1. A rise in the arterial and the venous pressure may occur, but the arterial pressure lasts only twelve hours. 2. The rise in arterial pressure does not depend on the effects of sympathetic innervation or release. (This disputes the theory of Leriche.) 3. The procedure did not affect the incidence of gangrene in his series of cases. 4. There may occur a richer collateral bed as a result of ligation, but it has no bearing on the nutrition of tissues or on the process of gangrene. 5. Ligation of the femoral vein may produce the dangerous effects of chronic venous stasis. 6. If the principle of venous ligation is to be practiced at all, temporary occlusion would be preferable.

Brooks, Johnson and Kirtley [23] sought to determine by experimental means the exact conditions constituting indications for ligation of the femoral vein following arterial obstruction. They repeated the work of Brooks and Martin [8] on rabbits, with the following results: In 100 experiments the arteries alone were ligated, with mass necrosis of the extremity resulting in 46 animals; in 100 experiments in which concomitant ligation of the vein was done with ligation of the artery, necrosis occurred in only 4 rabbits. However, when the arteries were injected with a radiopaque substance, there was not the same degree of arterial obstruction in any 2 rabbits. It was therefore difficult to evaluate by arteriographic evidence the changes occurring after ligation. They concluded that ligation of the vein had an extremely favorable influence on the incidence of gangrene but that the proof must rest essentially on clinical evidence.

Ligation of the femoral vein proximal to the saphenofemoral junction causes temporary edema. A small degree of this swelling may be due partly to reflex vasospasm and when recognized may be amenable to lumbar ganglion block with procaine hydrochloride. In my experience, ligation immediately distal to the junction of the vena profunda with the superficial femoral vein is free from subsequent edema. However, the degree of residual edema may be dependent on the presence or absence of venous thrombosis, which may have been present before the venous ligation or may have occurred afterward. Edema is also dependent on the number of functioning collateral vessels as noticed after ligation of the inferior vena cava, which in most instances is attended by less edema than when the common femoral vein is interrupted. The reason for this is evident in a review of the anatomy of the collateral veins in this region. Disagreement on this point by some can be traced to varied levels employed in ligation of the femoral vein. Silbert,[21] who practiced ligation of the common femoral vein, noted swelling on the day following operation. It was moderate and tended to

19. Pearse, H. E., Jr.: Use of Vein Ligation in Treatment of Arteriosclerotic and Diabetic Gangrene, J. A. M. A. **98**:866 (March 12) 1932.

20. McWhorter, G. L.: Ligation of Both Femoral Artery and Vein in Thromboangiitis Obliterans, S. Clin. North America **10**:283, 1930.

21. Silbert, S.: Value of Femoral Vein Ligation in Chronic Arterial Obstruction, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman, New York, International Press, 1932, vol. 3, p. 1079.

22. Wilson, W. C.: Occlusion of Main Artery and Main Vein of a Limb, Brit. J. Surg. **20**:393, 1933.

23. Brooks, B.; Johnson, G. S., and Kirtley, J. A., Jr.: Simultaneous Ligation: Experimental Study of Effect of Ligation of Concomitant Vein on Incidence of Gangrene Following Arterial Obstruction, Surg., Gynec. & Obst. **59**:496, 1934.

diminish. He stated that "some increase in the size of the leg occasionally persists, but has never been more than a few centimeters and has caused no discomfort or complaints." Homans [24] aptly summarized the resulting edema as follows:

> It should be recognized that whereas division of the superficial femoral vein for thrombosis confined to some group of deep veins below the knee is attended by little or no edema and cyanosis, the situation when the whole femoral system is occupied is very different; collateral pathways are perhaps involved, and division may cause serious edema.

Allen, Linton and Donaldson,[25] although they agreed that ligation of the femoral vein is a simple and effective procedure, stated that edema is the most common and most serious postoperative complication but may usually be controlled by the application of a woven bandage. Early swelling is more frequent after ligation of the common femoral vein, but late edema occurs with equal frequency after either superficial or common femoral interruption. In Veal's [26] cases, following amputation edema of the stump occurred only occasionally. He explained this complication as probably due to thrombosis in the profunda vein. However, even in these instances the edema subsided within ten days.

The experience with this series that there has been complete absence of pulmonary complications following ligation of the femoral vein, especially when amputation was performed subsequently, has been corroborated by Veal. He noted that pulmonary embolism has always been a common and dreaded complication following amputations on the thigh. By performing a prophylactic ligation of the femoral vein at the time of amputation, Veal has reduced this complication to almost zero. Of 275 cases of amputation without the benefit of ligation of the femoral vein, death due to pulmonary complications occurred in 14.9 per cent, while in 80 cases of amputation with ligation there was only 1 pulmonary complication. This low incidence is explained by the fact that the femoral vein below the vena profunda commonly receives only a few small branches, so that a low ligation would leave a column of blood with a sluggish circulation. With only a few small tributaries, the ascending clot might easily break off at an upper level, where the caliber of the femoral vein is increased.

Relief of pain following ligation of the femoral vein in the majority of the cases was mentioned in our preliminary report. Relief of pain is the result not only of increased collateral circulation with its attendant increased oxygenation of tissues. Division of the femoral vein must necessarily include partial interruption of sympathetic pathways. This is also a probable factor in relief of pain. In addition, there must be another factor, as yet not understood or explained as has been illustrated in cases of thromboangiitis obliterans in which there was relief of pain following ligation of the saphenous vein. This observation was made in 4 recent cases and also in 1 case of arteriosclerosis obliterans. In view of these findings, it might be of interest to see whether ligation of any isolated vein might not give identical results.

My technic for performing ligation of the femoral vein consists of interruption of the superficial femoral vein immediately distal to its junction with the vena profunda. The incision, 4 inches (10 cm.) in length, is placed over the course of the femoral artery starting at Poupart's ligament. Transfixion of the cut ends of the vein is a safeguard against slipping of the ligature.

ANALYSIS OF CASES

As might be expected, the condition in all of the patients without exception was complicated by systemic degenerative disease. This analysis includes 110 patients subjected to 118 ligations of the femoral vein—bilateral for 8 patients. Lesions on the feet or toes, such as ulcer, gangrene or cellulitis, were present in 88 (80 per cent) of the patients, outlined in table 1. The principal diagnoses made on the patients' admission to the hospital under the heading of peripheral vascular disease were arteriosclerosis complicated by diabetes (60 cases), arteriosclerosis obliterans (44 cases) and thromboangiitis obliterans (6 cases). The associated diseases observed on the patients' admission are listed in

TABLE 1.—*Incidence of Lesions on the Foot*

	Ulcers on Toes	Cellulitis	Moist Gangrene of Toes	Dry Gangrene of Toes
Diabetes with arteriosclerosis.	17	7	7	22
Arteriosclerosis obliterans.....	8	2	6	18
Thromboangiitis obliterans...	1	0	0	0

24. Homans, J.: Exploration and Division of the Femoral and Iliac Veins in the Treatment of Thrombophlebitis of the Leg, New England J. Med. **224**:179, 1941.

25. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Thrombosis and Embolism: Review of Two Hundred and Two Patients Treated by Femoral Vein Interruption, Ann. Surg. **118**:728, 1943.

26. Veal, J. R.: The Prevention of Pulmonary Complications Following Thigh Amputation by High Ligation of Femoral Vein, J. A. M. A. **121**:240 (Jan. 23) 1943; High Ligation of the Femoral Vein in Amputations of Lower Extremities, ibid. **114**:1616 (April 27) 1940.

table 2. The sex incidence was 43 women and 67 men. Of these, 60 were diabetic—33 women and 27 men. The age incidence showed the largest number of persons to be in the sixth decade—the youngest was 33 and the oldest 92 years (table 3). In addition to the operative procedures outlined in table 4, 30 amputations on the thigh were performed subsequent to ligation of the femoral vein. The lapse of time after the latter operation was one to two hundred and twenty days. Ten patients in this series were admitted with a previous amputation on the thigh. Pain as a prominent symptom on admission was noted in 61 patients. Relief for 50 (81.9 per cent) resulted following ligation of the femoral vein. The mortality in the hospital was in no instance associated with ligation of the vein. An analysis of the 20 deaths in this series (table 5) are attributed to intercurrent diseases.

An attempt at follow-up examinations in this series was successful for 75 of the 90 patients who were discharged from the hospital—15 could not be traced. As analyzed in table 6, the end results are divided according to the age group and the interval following ligation of the femoral vein.

TABLE 2.—*Associated Diseases Observed on Hospitalization*

	No. of Cases		No. of Cases
Pulmonary tuberculosis	2	Cardiac decompensation	8
Auricular fibrillation	6	Iliofemoral thrombophlebitis	4
Emphysema	10	Lymphogranuloma venereum	1
Arterial thrombosis	6	Hemiplegia	9
Coronary thrombosis	11	Asthma	5
Pleurisy	2	Cirrhosis of liver	8
Syphilis	9	Carcinoma of rectum	1

TABLE 3.—*Peripheral Vascular Diseases According to Age Distribution*

	Age Groups						
	30-39	40-49	50-59	60-69	70-79	80-89	90-99
Diabetes with arteriosclerosis	1	2	14	28	13	2	0
Arteriosclerosis obliterans	0	1	9	14	16	4	1
Thromboangiitis obliterans	2	1	2	1	0	0	0

TABLE 4.—*Additional Operative Procedures*

	No. of Cases
Amputation of toe	15
Incision and drainage	11
Periarterial sympathectomy	45
Ligation of femoral artery	2
Lumbar ganglionectomy	6
Resection of femoral artery	1
Neurectomy for pain	5
Excision of infected callus	4
Arteriography	24

TABLE 5.—*Analysis of Twenty Deaths Occurring in the Hospital*

Age	Postoperative Days	Cause of Death
60	60	Pneumonia and nephrosis
75	46	Uremia
63	60	Coronary thrombosis
68	3	Coronary thrombosis
67	5	Coronary thrombosis
79	41	Cardiac decompensation
72	7	Sepsis—refused operation
76	58	Cerebral embolism
56	30	Pneumonia—tuberculosis
64	12	Cerebral thrombosis
82	15	Cerebral thrombosis
65	28	Coronary thrombosis
50	5	Cerebral thrombosis
70	46	Sepsis—refused amputation
78	86	Sepsis—refused amputation
51	5	Uremia
74	30	Sepsis—refused amputation
57	65	Sepsis—refused amputation
62	13	Cardiac decompensation
74	12	Cardiac decompensation

TABLE 6.—*Data on Follow-Up Examinations in Seventy-Five Cases*

Age Group	Postoperative Interval in Years	No. of Cases	Result
30 to 39	5	1	Alive and well
	3	1	Alive and well
	2	1	Amputation—thromboangiitis obliterans
40 to 49	4	1	Alive and well
	4	1	Alive and well
	4	1	Alive and well
	2	1	Alive and well
50 to 59	5	9	Amputation for 2; 7 alive and well
	4	3	Amputation for 1; 2 alive and well
	3	1	Amputation
	2	5	Died of "heart disease"
	1	1	Died of sepsis—amputation refused
60 to 69	5	4	Amputation for 2
	4	2	Alive and well
	3	8	Amputation for 3
	2	8	4 died—"heart disease"; 4 had sepsis and gangrene
	1	6	5 died—"heart disease"; 1 had sepsis and gangrene
70 to 79	4	4	Amputation for 1
	3	2	Amputation for 1
	2	4	4 died—"senility"; 1 had sepsis and gangrene
	1	4	2 died—"senility"; 2 had sepsis and gangrene
80 to 89	2	2	1 alive and well; 1 died—"senility"
	1	1	Died—sepsis and gangrene
	½	2	2 died after amputation
92	½	1	Died—"senility"

COMMENT

In accordance with physiologic principles and clinical experience, ligation of the femoral vein is a valuable procedure in selected cases, as discussed in the previous review of the literature and the

ligatures done in the Flower and Fifth Avenue Hospitals and the Metropolitan Hospital. In order to determine indications for the procedure and a proper selection of cases, ligation of the femoral vein was performed on all patients with chronic obstructive arterial disease who consented to the operation. As a result, the series included patients whose condition was unfavorable or "hopeless" in view of such complications as spreading gangrene and sepsis. However, ligation of the femoral vein was of definite value in the prevention of gangrene and the alleviation of pain. Increased collateral circulation was evidenced by increased bleeding which was noted at amputation following ligation of the femoral vein and also by means of arteriography. In 6 of the patients, the pulses became palpable postoperatively. The absence of pulmonary embolism as a complication following amputation has also been noted. Ligation distal to the entrance of the profunda vein is probably the reason why edema was absent in these patients. Thrombosis has never been noticed in the femoral vein proximal to the site of ligation because large tributaries in this region associated with a swift stream of venous blood obviate this complication. Final follow-up examinations of those patients who were found alive (38.6 per cent, or 29 patients) showed that of these 17 required amputation. In this group, 14 had been admitted to the hospital with gangrene or ulcers on the toes, while of the 12 who remained alive and well 8 had been hospitalized with these same lesions. In other words, 88 of the 110 patients were admitted with active lesions on the toes; this showed that the greatest number of patients were treated after the phase in which ligation of the femoral vein might be considered prophylactic. However, 25.4 per cent of the entire series were alive at the time of the final follow-up examination. It might be reasonable to expect that had ligation of the femoral vein been performed as a prophylactic measure only, the statistical figures would have been more impressive. Since no morbidity or mortality is associated with the procedure of ligation of the femoral vein this operation should be employed more commonly in selected cases, as suggested previously.

SUMMARY

Ligation of the femoral vein is definitely indicated for prophylaxis in chronic obstructive arterial disease—before such lesions as gangrene, ulceration and infection present themselves.

Ligation of the femoral vein is not associated with morbidity or mortality.

Relief of pain was obtained in the majority of the cases.

The prevention of subsequent pulmonary embolism following amputation is definite.